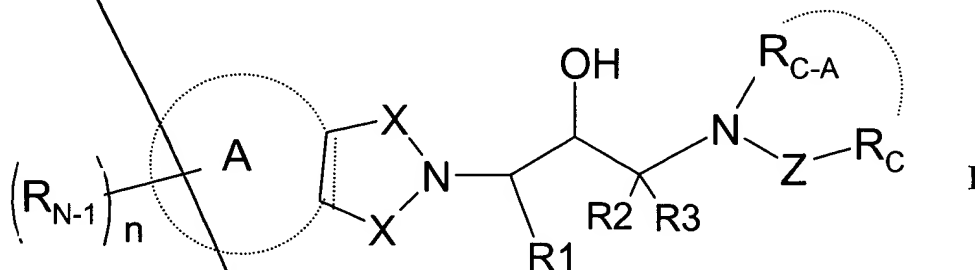


We claim:

1) A disubstituted amine of formula I



where  $R_1$  is:

(I)  $C_1$ - $C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl,  $C_1$ - $C_7$  alkyl (optionally substituted with  $C_1$ - $C_3$  alkyl and  $C_1$ - $C_3$  alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C $\equiv$ N, -CF $_3$ ,  $C_1$ - $C_3$  alkoxy, -NR $_{1-a}$ R $_{1-b}$  where R $_{1-a}$  and R $_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl, and -OC=O NR $_{1-a}$ R $_{1-b}$  where R $_{1-a}$  and R $_{1-b}$  are as defined above,

(II) -CH $_2$ -S(O) $_{0-2}$ -( $C_1$ - $C_6$  alkyl),

(III) -CH $_2$ -CH $_2$ -S(O) $_{0-2}$ -( $C_1$ - $C_6$  alkyl),

(IV)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF $_3$ ,  $C_1$ - $C_3$  alkoxy, and -NR $_{1-a}$ R $_{1-b}$  where R $_{1-a}$  and R $_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,

(V)  $C_2$ - $C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF $_3$ ,  $C_1$ - $C_3$  alkoxy, and -NR $_{1-a}$ R $_{1-b}$  where R $_{1-a}$  and R $_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,

(VI) -(CH $_2$ ) $_{n_1}$ -(R $_{1-aryl}$ ) where  $n_1$  is zero or one and where R $_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C $\equiv$ N, -CF $_3$ ,  $C_1$ - $C_3$  alkoxy, and -NR $_{1-a}$ R $_{1-b}$  where R $_{1-a}$  and R $_{1-b}$  are as defined above,

(B) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(D) -F, -Cl, -Br or -I,

(F) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(G) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(H) -OH,

(I) -C≡N,

(J) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(K) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(L) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(M) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(N) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heteroaryl</sub>) where n<sub>1</sub> is as defined above and where R<sub>1-heteroaryl</sub> is selected from the group consisting of:

pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoquinolyl,

F02C3/00

quinazolinyI,  
quinoxalinyI,  
phthalazinyI,  
imidazolyl,  
isoxazolyl,  
pyrazolyl,  
oxazolyl,  
thiazolyl,  
indolizinyI,  
indazolyl,  
benzothiazolyl,  
benzimidazolyl,  
benzofuranyl,  
furanyl,  
thienyl,  
pyrrolyl,  
oxadiazolyl,  
thiadiazolyl,  
triazolyl,  
tetrazolyl,  
oxazolopyridinyI,  
imidazopyridinyI,  
isothiazolyl,  
naphthyridinyI,  
cinnolinyI,  
carbazolyl,  
beta-carbolinyI,  
isochromanyl,  
chromanyl,  
tetrahydroisoquinolinyI,  
isoindolinyI,



F06E30/00

dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,  
indolinyl N-oxide,  
isoquinolyl N-oxide,  
quinazolinyl N-oxide,  
quinoxalinyl N-oxide,  
phthalazinyl N-oxide,  
imidazolyl N-oxide,  
isoxazolyl N-oxide,  
oxazolyl N-oxide,  
thiazolyl N-oxide,  
indolizinyl N-oxide,  
indazolyl N-oxide,  
benzothiazolyl N-oxide,  
benzimidazolyl N-oxide,  
pyrrolyl N-oxide,  
oxadiazolyl N-oxide,  
thiadiazolyl N-oxide,  
triazolyl N-oxide,  
tetrazolyl N-oxide,  
benzothiopyranyl S-oxide, and  
benzothiopyranyl S,S-dioxide,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{n1}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four:

- (1)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (2)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1$ - $C_6$  alkyl,
- (3)  $C_2$ - $C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1$ - $C_6$  alkyl,
- (4)  $-F$ ,  $Cl$ ,  $-BR$ , or  $-I$ ,
- (6)  $C_1$ - $C_6$  alkoxy optionally substituted with one, two, or three  $-F$ ,
- (7)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined below,
- (8)  $-OH$ ,
- (9)  $-C\equiv N$ ,
- (10)  $C_3$ - $C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1$ - $C_6$  alkyl,
- (11)  $-CO-(C_1-C_4 \text{ alkyl})$ ,
- (12)  $-SO_2-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (13)  $-CO-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, or
- (14)  $-SO_2-(C_1-C_4 \text{ alkyl})$ , with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$

is not bonded to the carbon chain by nitrogen, or

(VIII)  $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and  $R_{1\text{-heterocycle}}$  is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,  
thiomorpholinyl S-oxide,  
thiomorpholinyl S,S-dioxide,  
piperazinyl,  
homopiperazinyl,  
pyrrolidinyl,  
pyrrolinyl,  
tetrahydropyranyl,  
piperidinyl,  
tetrahydrofuranyl,  
tetrahydrothienyl,  
homopiperidinyl,  
homomorpholinyl,  
homothiomorpholinyl,  
homothiomorpholinyl S,S-dioxide,  
oxazolidinonyl,  
dihydropyrazolyl,  
dihydropyrrolyl,  
dihydropyrazinyl,  
dihydropyridinyl,  
dihydropyrimidinyl,  
dihydrofuryl,  
dihydropyranyl,  
tetrahydrothienyl S-oxide,  
tetrahydrothienyl S,S-dioxide, and  
homothiomorpholinyl S-oxide,

where the R<sub>1</sub>-heterocycle group is bonded by any atom of the parent R<sub>1</sub>-heterocycle group substituted by hydrogen such that the new bond to the R<sub>1</sub>-heterocycle group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(3) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(4) -F, Cl, -Br, or -I,

(5) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(6) -C<sub>1</sub>-C<sub>6</sub> alkoxy substituted with one, two, or three -F,

(7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(8) -OH,

(9) -C≡N,

(10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), or

(15) =O, with the proviso that when n<sub>1</sub> is zero R<sub>1-heterocycle</sub> is not bonded to the carbon chain by nitrogen;

where R<sub>2</sub> is:

(I)-H,



(II) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub> where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above;

(IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, or

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

where R<sub>3</sub> is:

(I)-H,

(II) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub> where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above;

(IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, or

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

where R<sub>2</sub> and R<sub>3</sub> are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO<sub>2</sub>-, and -NR<sub>N-2</sub>-,

where  $R_{N-2}$  is selected from the group consisting of:

- (a) -H,
- (b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of:
  - (i) -OH, and
  - (ii) -NH<sub>2</sub>,
- (c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
- (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
- (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
- (g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,
- (h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,
- (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
- (j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and
- (k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above;

where X is independently chosen from the group consisting of:

- C(O)-,
- CH<sub>2</sub>-,
- CH<sub>2</sub>-CH<sub>2</sub>-, and
- CH<sub>2</sub>-C(O)-;

wherein in the rings drawn, a dotted line indicates an optional double bond or an optional ring;

wherein ring A is phenyl, cyclohexyl, cyclopentyl, pyridyl, pyrimidinyl, pyrazinyl or is absent; and

where  $R_{N-1}$  is selected from the group consisting of:

- (1) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I,

-OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2) -OH,

(3) -NO<sub>2</sub>,

(4) -F, -Cl, -Br, or -I,

(5) -CO-OH,

(6) -C≡N,

(7) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are selected from the group consisting of:

(a) -H,

(b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH<sub>2</sub>,

(c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

(d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(e) -(C<sub>1</sub>-C<sub>3</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),

(g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,

(i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,

(j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and

(k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,

(8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),

(9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two, or three double bonds),

(10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two, or three triple bonds),

(11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

- above,
- (12)  $-(CH_2)_{0-4}-CO-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,
- (13)  $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,
- (14)  $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,
- (15)  $-(CH_2)_{0-4}-CO-R_{N-4}$  where  $R_{N-4}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homoythiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of:  $C_1-C_6$  alkyl,
- (16)  $-(CH_2)_{0-4}-CO-O-R_{N-5}$  where  $R_{N-5}$  is selected from the group consisting of:
- above,
- (a)  $C_1-C_6$  alkyl,
- (b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,
- (c)  $C_2-C_6$  alkenyl containing one, or two double bonds,
- (d)  $C_2-C_6$  alkynyl containing one, or two triple bonds,
- (e)  $C_3-C_7$  cycloalkyl, and
- (f)  $-(CH_2)_{0-2}-(R_{1-heteroaryl})$  where  $R_{1-heteroaryl}$  is as defined above,
- defined above,
- (17)  $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,
- (18)  $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$ ,
- (19)  $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$ ,
- (20)  $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$ ,
- (21)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$  where  $R_{N-5}$  can be the same or different and is as defined above,
- (22)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$ , where  $R_{N-5}$  can be the same or different and is as defined above,

(23)  $-(\text{CH}_2)_{0-4}-\text{N}-\text{CS}-\text{N}(\text{R}_{\text{N}-5})_2$ , where  $\text{R}_{\text{N}-5}$  can be the same or different and is as defined above,

(24)  $-(\text{CH}_2)_{0-4}-\text{N}(-\text{H} \text{ or } \text{R}_{\text{N}-5})-\text{CO}-\text{R}_{\text{N}-2}$  where  $\text{R}_{\text{N}-5}$  and  $\text{R}_{\text{N}-2}$  can be the same or different and are as defined above,

(25)  $-(\text{CH}_2)_{0-4}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  can be the same or different and are as defined above,

(26)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,

(27)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(28)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{P}(\text{O})-(\text{OR}_{\text{N-aryl-1}})_2$  where  $\text{R}_{\text{N-aryl-1}}$  is  $-\text{H}$  or  $\text{C}_1-\text{C}_4$  alkyl,

(29)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{CO}-\text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(30)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{CS}-\text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(31)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(32)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2-\text{COOH}$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(33)  $-(\text{CH}_2)_{0-4}-\text{S}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(34)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl})$  optionally substituted with one, two, three, four, or five of:  $-\text{F}$ ,

(35)  $\text{C}_3-\text{C}_7$  cycloalkyl,

(36)  $\text{C}_2-\text{C}_6$  alkenyl with one or two double bonds optionally substituted with  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_3$  alkoxy, or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(37)  $\text{C}_2-\text{C}_6$  alkynyl with one or two triple bonds optionally substituted with  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_3$  alkoxy, or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(38)  $-(\text{CH}_2)_{0-4}-\text{N}(-\text{H} \text{ or } \text{R}_{\text{N}-5})-\text{SO}_2-\text{R}_{\text{N}-2}$  where  $\text{R}_{\text{N}-5}$  and  $\text{R}_{\text{N}-2}$  can be the same or different and are as described above, and

(39)  $-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7$  cycloalkyl;

where n is equal to 0, 1, 2 or 3;

where Z is selected from the group consisting of:

- (A)  $-\text{C}(\text{O})-$ ,
- (B)  $-\text{S}(\text{O})_{1-2}-$ ,
- (C)  $-\text{C}(\text{O})-\text{X}_{\text{N}-1}-$  where  $\text{X}_{\text{N}-1}$  is selected from the group consisting of  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'$  and where  $\text{R}'$  is as defined above; and
- (D) a single bond;

where  $\text{R}_\text{C}$  is:

(I)  $\text{C}_1\text{-C}_{10}$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $-\text{O}$ -phenyl,  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  $-\text{OC}=\text{O NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  $-\text{S}(=\text{O})_{0-2} \text{R}_{1-a}$  where  $\text{R}_{1-a}$  is as defined above,  $-\text{NR}_{1-a}\text{C}=\text{O NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  $-\text{C}=\text{O NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above, and  $-\text{S}(=\text{O})_2 \text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(II)  $-(\text{CH}_2)_{0-3}\text{-(C}_3\text{-C}_8)$  cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $-\text{O}$ -phenyl,  $-\text{CO-OH}$ ,  $-\text{CO-O-(C}_1\text{-C}_4 \text{ alkyl)}$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(III)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}\text{-R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are

- (A)  $-\text{H}$ ,
- (B)  $\text{C}_1\text{-C}_4$  alkyl optionally substituted with one or two  $-\text{OH}$ ,
- (C)  $\text{C}_1\text{-C}_4$  alkoxy optionally substituted with one, two, or three  $-\text{F}$ ,
- (D)  $-(\text{CH}_2)_{0-4}\text{-C}_3\text{-C}_7$  cycloalkyl,
- (E)  $\text{C}_2\text{-C}_6$  alkenyl containing one or two double bonds,
- (F)  $\text{C}_2\text{-C}_6$  alkynyl containing one or two triple bonds,
- (G) phenyl-,
- (H)  $\text{C}_0\text{-C}_4$  alkyl  $\text{C}(\text{O}) \text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined

above,

and where  $R_{C-x}$  and  $R_{C-y}$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-SO_2-$ ,  $-NR_{N-2}-$  and  $R_{C-aryl}$  is the same as  $R_{N-aryl}$  and where  $R_{C-aryl}$  may optionally be substituted with  $-C_0-C_4$  alkyl- $C(O)NR_{1-a}R_{1-b}$ ,  $C_0-C_4$  alkyl- $C(O)OR_{1-a}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(IV)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is the same as  $R_{N-heteroaryl}$  and  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(V)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$  where  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$  where  $R_{C-aryl}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(IX)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-heterocycle}$ , and  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(X)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$  where  $R_{C-heteroaryl}$ ,  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIV)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$ , and  $R_{C-y}$  are as defined above,

(XV)  $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$  where  $R_{C-3}$  is as defined below and  $R_{C-1}$ ,  $R_{C-2}$  are the same or different and are selected from the group consisting of:

(A) -H,

(B) -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two, or three substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one, or two double bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(F) -(CH<sub>2</sub>)<sub>1-2</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(F) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(G) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined for R<sub>1-aryl</sub>,

(H) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(I) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(J) -R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(K) -R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(M) -(CH<sub>2</sub>)<sub>1-4</sub>-R<sub>C-4</sub>-(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C'-aryl</sub> where R<sub>C-4</sub> is -O-, -S- or -NR<sub>C-5</sub>- where R<sub>C-5</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, and where R<sub>C'-aryl</sub> is defined above,

(N) -(CH<sub>2</sub>)<sub>1-4</sub>-R<sub>C-4</sub>-(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-4</sub> and R<sub>C-heteroaryl</sub> are as defined above, and

(O) -R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined above,

and where R<sub>C-3</sub> is the same or different and is:

(a) -H,



(b)  $\text{-C}_1\text{-C}_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ ,  $\text{-I}$ ,  $\text{-OH}$ ,  $\text{-SH}$ ,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $\text{-O-phenyl}$ , and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(c)  $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ ,  $\text{-I}$ ,  $\text{-OH}$ ,  $\text{-SH}$ ,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $\text{-O-phenyl}$ , and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(d)  $\text{C}_2\text{-C}_6$  alkynyl with one, or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ ,  $\text{-I}$ ,  $\text{-OH}$ ,  $\text{-SH}$ ,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $\text{-O-phenyl}$ , and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(e)  $\text{-(CH}_2\text{)}_{0-4}\text{-C}_3\text{-C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ ,  $\text{-I}$ ,  $\text{-OH}$ ,  $\text{-SH}$ ,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $\text{-O-phenyl}$ , and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(f)  $\text{-R}_{\text{C}'\text{-aryl}}$  where  $\text{R}_{\text{C}'\text{-aryl}}$  is as defined above,

(g)  $\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(h)  $\text{-R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(i)  $\text{-(C}_1\text{-C}_4\text{ alkyl)-R}_{\text{C}'\text{-aryl}}$  where  $\text{R}_{\text{C}'\text{-aryl}}$  is as defined above,

(j)  $\text{-(C}_1\text{-C}_4\text{ alkyl)-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(k)  $\text{-(C}_1\text{-C}_4\text{ alkyl)-R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(XVI)  $\text{-CH(R}_{\text{C-aryl}}\text{)}_2$  where  $\text{R}_{\text{C-aryl}}$  are the same or different and are as defined above,

(XVII)  $\text{-CH(R}_{\text{C-heteroaryl}}\text{)}_2$  where  $\text{R}_{\text{C-heteroaryl}}$  are the same or different and are as defined above,

(XVIII)  $\text{-CH(R}_{\text{C-aryl}}\text{)(R}_{\text{C-heteroaryl}}\text{)}$  where  $\text{R}_{\text{C-aryl}}$  and  $\text{R}_{\text{C-heteroaryl}}$  are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$  where  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$  are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH,  $NR_{N-5}$ , O, or  $S(=O)_{0-2}$ , and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one, or two  $-C_1-C_3$  alkyl,  $-F$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $=O$ , or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XX)  $C_2-C_{10}$  alkenyl containing one or two double bonds optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $C_2-C_{10}$  alkynyl containing one, or two triple bonds optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $-(CH_2)_{0-1}-CH(R_{C-6})-(CH_2)_{0-1}-R_{C-aryl}$  where  $R_{C-aryl}$  is as defined above and  $R_{C-6}$  is  $-(CH_2)_{0-6}-OH$ ,

(XXII)  $-(CH_2)_{0-1}-CH(R_{C-6})-(CH_2)_{0-1}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  and  $R_{C-6}$  is as defined above,

(XXIII)  $-CH(-R_{C-aryl} \text{ or } R_{C-heteroaryl})-CO-O(C_1-C_4 \text{ alkyl})$  where  $R_{C-aryl}$  and  $R_{C-heteroaryl}$  are as defined above,

(XXIV)  $-CH(-CH_2-OH)-CH(-OH)-phenyl-NO_2$ ,

(XXV)  $(C_1-C_6 \text{ alkyl})-O-(C_1-C_6 \text{ alkyl})-OH$ ,

(XXVII)  $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$ , or

(XXVIII)  $-(CH_2)_{0-6}-C(=NR_{1-a})(NR_{1-a}R_{1-b})$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

where  $R_{C-A}$  is H,  $C_1-C_{10}$  alkyl,  $C_2-C_{10}$  alkenyl and alkynyl, phenyl,  $C_1-C_4$  alkyl- $R_{N-aryl}$ ,  $C_1-C_4$  alkyl- $R_{N-heteroaryl}$ ,  $C_1-C_4$  alkyl- $C_3-C_7$  cycloalkyl, or  $C_1-C_4$  alkyl- $R_{1-heterocycle}$ , wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-$

SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy,  $-C(O)O-R_{1-a}$ , and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$ ,  $C_1-C_6$  alkyl or phenyl;

where  $R_{C-A}$ ,  $-Z-R_C$ , and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1)  $C_1-C_6$  alkyl,  
 $C_2-C_6$  alkenyl with one or two double bonds, or  
 $C_2-C_6$  alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

(2)  $-F$ ,  $Cl$ ,  $-Br$ , or  $-I$ ,

(3)  $-C_1-C_6$  alkoxy optionally substituted with one, two, or three  $-F$ ,

(4)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined below,

(5)  $-OH$ ,

(6)  $-C\equiv N$ ,

(7)  $=O$  (oxo),

(8)  $-CO-(C_1-C_4 \text{ alkyl})$ ,

(9)  $-SO_2-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, or

(10)  $-CO-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

or a pharmaceutically acceptable salt thereof.

2. A disubstituted amine of claim 1, wherein  $R_1$  is:

$-(CH_2)_{0-1}-(R_{1-aryl})$ , or

$-(CH_2)_{n1}-(R_{1-heteroaryl})$ .

3. A disubstituted amine of claim 2, wherein  $R_1$  is:

$-(CH_2)-(R_{1-aryl})$ , or  
 $-(CH_2)-(R_{1-heteroaryl})$ .

4. A disubstituted amine of claim 3, wherein  $R_1$  is  $-(CH_2)-(R_{1-aryl})$  where  $R_{1-aryl}$  is phenyl.
5. A disubstituted amine of claim 4, wherein  $R_1$  is substituted with two  $-F$ .
6. A disubstituted amine of claim 5, wherein the  $-F$  substitutions is on the -3 and -5 positions.
7. A disubstituted amine of claim 1, wherein  $R_2$  and  $R_3$  are both  $-H$ .
8. A disubstituted amine of claim 1, wherein  $R_C$  is:
  - $-C_1-C_8$  alkyl,
  - $-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ , or
  - cyclopentyl or -cyclohexyl ring fused to  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .
9. A disubstituted amine of claim 8, wherein  $R_C$  is:
  - $-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ ,
  - cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .
10. A disubstituted amine of claim 9, wherein  $R_C$  is:
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,
  - $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,
  - cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

11. A disubstituted amine of claim 10, wherein  $R_C$  is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-aryl}$  is phenyl.

12. A disubstituted amine of claim 11, wherein said phenyl is substituted in the 3-position or 3,5-positions.

13. A disubstituted amine of claim 1, wherein  $R_{C-A}$  is:

-methyl, or

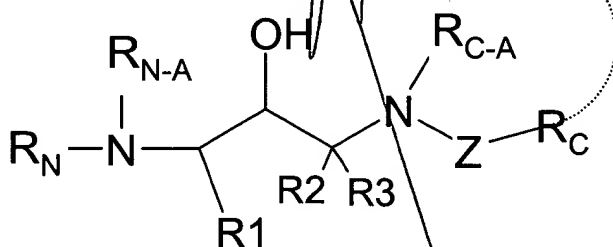
-ethyl.

14. A disubstituted amine of claim 1, wherein Z is:

$-C(O)-$ , or

$-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of  $-O-$ ,  $-S-$  and  $-NR'-$ .

15. A disubstituted amine of formula II



II

where  $R_1$  is:

(I)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $C_1-C_7$  alkyl (optionally substituted with  $C_1-C_3$  alkyl and  $C_1-C_3$  alkoxy),  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,

-SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, and -OC=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(II) -CH<sub>2</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(III) -CH<sub>2</sub>-CH<sub>2</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(VI) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-aryl</sub>) where n<sub>1</sub> is zero or one and where R<sub>1-aryl</sub> is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(B) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(D) -F, Cl, -Br or -I,

(F) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(G) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(H) -OH,

(I) -C≡N,

(J) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(K) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(L) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(M) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(N) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heteroaryl</sub>) where n<sub>1</sub> is as defined above and where R<sub>1-heteroaryl</sub> is selected from the group consisting of:

pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoquinolyl,  
quinazolinyl,  
quinoxalinyl,  
phthalazinyl,  
imidazolyl,  
isoxazolyl,  
pyrazolyl,  
oxazolyl,  
thiazolyl,  
indolizinyl,  
indazolyl,  
benzothiazolyl,  
benzimidazolyl,  
benzofuranyl,

furanyl,  
thienyl,  
pyrrolyl,  
oxadiazolyl,  
thiadiazolyl,  
triazolyl,  
tetrazolyl,  
oxazolopyridinyl,  
imidazopyridinyl,  
isothiazolyl,  
naphthyridinyl,  
cinnolinyll,  
carbazolyl,  
beta-carbolinyl,  
isochromanyl,  
chromanyl,  
tetrahydroisoquinolinyll,  
isoindolinyll,  
isobenzotetrahydrofuranyl,  
isobenzotetrahydrothienyl,  
isobenzothienyl,  
benzoxazolyl,  
pyridopyridinyl,  
benzotetrahydrofuranyl,  
benzotetrahydrothienyl,  
purinyl,  
benzodioxolyl,  
triazinyl,  
phenoxazinyl,  
phenothiazinyl,  
pteridinyl,



benzothiazolyl,  
imidazopyridinyl,  
imidazothiazolyl,  
dihydrobenzisoaxazinyl,  
benzisoaxazinyl,  
benzoxazinyl,  
dihydrobenzisothiazinyl,  
benzopyranyl,  
benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromonyl,  
chromanonyl,  
pyridinyl-N-oxide,  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisoquinolinonyl  
dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,  
indolinyl N-oxide,  
isoquinolyl N-oxide,

quinazoliny N-oxide,  
 quinoxaliny N-oxide,  
 phthalaziny N-oxide,  
 imidazolyl N-oxide,  
 isoxazolyl N-oxide,  
 oxazolyl N-oxide,  
 thiazolyl N-oxide,  
 indoliziny N-oxide,  
 indazolyl N-oxide,  
 benzothiazolyl N-oxide,  
 benzimidazolyl N-oxide,  
 pyrrolyl N-oxide,  
 oxadiazolyl N-oxide,  
 thiadiazolyl N-oxide,  
 triazolyl N-oxide,  
 tetrazolyl N-oxide,  
 benzothiopyranyl S-oxide, and  
 benzothiopyranyl S,S-dioxide,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{n1}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four:

(1)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(2)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,

(3)  $C_2$ - $C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -

Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(4) -F, Cl, -BR, or -I,

(6) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(8) -OH,

(9) -C≡N,

(10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), with the proviso that when n<sub>1</sub> is zero R<sub>1</sub>-

heteroaryl is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heterocycle</sub>) where n<sub>1</sub> is as defined above and R<sub>1-heterocycle</sub> is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

pyrrolidinyl,

pyrrolinyl,

tetrahydropyranyl,

piperidinyl,

tetrahydrofuranyl,

tetrahydrothienyl,

homopiperidinyl,

homomorpholinyl,

homothiomorpholinyl,  
 homothiomorpholinyl S,S-dioxide,  
 oxazolidinonyl,  
 dihydropyrazolyl,  
 dihydropyrrolyl,  
 dihydropyrazinyl,  
 dihydropyridinyl,  
 dihydropyrimidinyl,  
 dihydrofuryl,  
 dihydropyranyl,  
 tetrahydrothienyl S-oxide,  
 tetrahydrothienyl S,S-dioxide, and  
 homothiomorpholinyl S-oxide,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heterocycle}}$  group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1)  $C_1\text{-}C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1\text{-}C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2)  $C_2\text{-}C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(3)  $C_2\text{-}C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(4) -F, Cl, -Br, or -I,

(5)  $C_1\text{-}C_6$  alkoxy,

(6)  $C_1\text{-}C_6$  alkoxy substituted with one, two, or three -F,

- (7)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are as defined below,  
 (8)  $-\text{OH}$ ,  
 (9)  $-\text{C}\equiv\text{N}$ ,  
 (10)  $\text{C}_3$ - $\text{C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1$ - $\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1$ - $\text{C}_6$  alkyl,  
 (11)  $-\text{CO}-(\text{C}_1$ - $\text{C}_4$  alkyl),  
 (12)  $-\text{SO}_2-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  
 (13)  $-\text{CO}-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  
 (14)  $-\text{SO}_2-(\text{C}_1$ - $\text{C}_4$  alkyl), or  
 (15)  $=\text{O}$ , with the proviso that when  $n_1$  is zero  $\text{R}_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $\text{R}_2$  is:

- (I)  $-\text{H}$ ,  
 (II)  $\text{C}_1$ - $\text{C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1$ - $\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1$ - $\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  
 (III)  $-(\text{CH}_2)_{0-4}-\text{R}_{2-1}$  where  $\text{R}_{2-1}$  is  $\text{R}_{1\text{-aryl}}$  or  $\text{R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-aryl}}$  and  $\text{R}_{1\text{-heteroaryl}}$  are as defined above;  
 (IV)  $\text{C}_2$ - $\text{C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1$ - $\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1$ - $\text{C}_6$  alkyl,  
 (V)  $\text{C}_2$ - $\text{C}_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1$ - $\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1$ - $\text{C}_6$  alkyl, or  
 (VI)  $-(\text{CH}_2)_{0-4}-\text{C}_3$ - $\text{C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1$ - $\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1$ - $\text{C}_6$  alkyl,

where  $R_3$  is selected from the group consisting of:

- (I) -H,
- (II)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (III)  $-(CH_2)_{0-4}-R_{2-1}$  where  $R_{2-1}$  is  $R_{1-aryl}$  or  $R_{1-heteroaryl}$  where  $R_{1-aryl}$  and  $R_{1-heteroaryl}$  are as defined above;
- (IV)  $C_2-C_6$  alkenyl with one or two double bonds,
- (V)  $C_2-C_6$  alkynyl with one or two triple bonds, or
- (VI)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1-C_6$  alkyl,

and where  $R_2$  and  $R_3$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-,  $-SO_2-$ , and  $-NR_{N-2}-$ ,

where  $R_{N-2}$  is selected from the group consisting of:

- (a) -H,
- (b)  $C_1-C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:
  - (i) -OH, and
  - (ii)  $-NH_2$ ,
- (c)  $C_1-C_6$  alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
- (d)  $C_3-C_7$  cycloalkyl,
- (e)  $-(C_1-C_2 \text{ alkyl})-(C_3-C_7 \text{ cycloalkyl})$ ,
- (f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,
- (g)  $C_2-C_6$  alkenyl with one or two double bonds,
- (h)  $C_2-C_6$  alkynyl with one or two triple bonds,

triple bond,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, and

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above;

where  $R_N$  is:

(I)  $R_{N-1}-X_N-$  where  $X_N$  is selected from the group consisting of:

(A)  $-CO-$ ,

(B)  $-SO_2-$ ,

(C)  $-(CR'R'')_{1-6}$  where  $R'$  and  $R''$  are the same or different and are  $-H$  or  $C_1-C_4$  alkyl,

(D)  $-CO-(CR'R'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is selected from the group consisting of  $-O-$ ,  $-S-$  and  $-NR'-$  and where  $R'$  and  $R''$  are as defined above, and

(E) a single bond;

where  $R_{N-1}$  is selected from the group consisting of:

(A)  $R_{N-aryl}$  where  $R_{N-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, or dihydronaphthyl optionally substituted with one, two or three of the following substituents which can be the same or different and are:

(1)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(2)  $-OH$ ,

(3)  $-NO_2$ ,

(4)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,

(5)  $-CO-OH$ ,

(6)  $-C\equiv N$ ,

(7)  $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are selected from the group consisting of:

- (a) -H,
- (b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of:
- (i) -OH, and
- (ii) -NH<sub>2</sub>,
- (c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
- (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
- (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
- (g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,
- (h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,
- (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
- (j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and
- (k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,
- (8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),
- (9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two or three double bonds),
- (10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two or three triple bonds),
- (11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (12) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above,
- (13) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,
- (14) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as defined above,
- (15) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is



optionally substituted with one, two, three, or four of: C<sub>1</sub>-C<sub>6</sub> alkyl,

(16)  $-(CH_2)_{0-4}-CO-O-R_{N-5}$  where R<sub>N-5</sub> is selected from the group

consisting of:

(a) C<sub>1</sub>-C<sub>6</sub> alkyl,

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where R<sub>1-aryl</sub> is as defined

above,

(c) C<sub>2</sub>-C<sub>6</sub> alkenyl containing one or two double

bonds,

(d) C<sub>2</sub>-C<sub>6</sub> alkynyl containing one or two triple

bonds,

(e) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(f)  $-(CH_2)_{0-2}-(R_{1-heteroaryl})$  where R<sub>1-heteroaryl</sub> is as

defined above,

(17)  $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$  where R<sub>N-2</sub> and R<sub>N-3</sub> are as

defined above,

(18)  $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$ ,

(19)  $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$ ,

(20)  $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$ ,

(21)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$  where R<sub>N-5</sub> can be the same or different and is as defined above,

(22)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$ , where R<sub>N-5</sub> can be the same or different and is as defined above,

(23)  $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$ , where R<sub>N-5</sub> can be the same or different and is as defined above,

(24)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$  where R<sub>N-5</sub> and R<sub>N-2</sub> can be the same or different and are as defined above,

(25)  $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$  where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or different and are as defined above,

(26)  $-(CH_2)_{0-4}-R_{N-4}$  where R<sub>N-4</sub> is as defined above,

(27)  $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$ ,

C<sub>1</sub>-C<sub>4</sub> alkyl,

(28)  $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$  where  $R_{N-aryl-1}$  is -H or

above,

(29)  $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined

above,

(30)  $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined

above,

(31)  $-(CH_2)_{0-4}-O-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(32)  $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$  where  $R_{N-5}$  is as defined

one, two, three, four, or five -F),

(33)  $-(CH_2)_{0-4}-S-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(34)  $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with}$

(35) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(36) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds optionally substituted with C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, or -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(37) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds optionally substituted with C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, or -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(38)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as described above, or

(39)  $-(CH_2)_{0-4}-C_3-C_7 \text{ cycloalkyl,}$

(B) -R<sub>N-heteroaryl</sub>, where R<sub>N-heteroaryl</sub> is selected from the group as defined above in R<sub>1-heteroaryl</sub> and where the R<sub>N-heteroaryl</sub> group is bonded by any atom of the parent R<sub>N-heteroaryl</sub> group substituted by hydrogen such that the new bond to the R<sub>N-heteroaryl</sub> group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

- (2) -OH,  
 (3) -NO<sub>2</sub>,  
 (4) -F, -Cl, -Br, or -I,  
 (5) -CO-OH,  
 (6) -C≡N,  
 (7) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the

same or different and are selected from the group consisting of:

- (a) -H,  
 (b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one

substituent selected from the group consisting of:

- (i) -OH, and  
 (ii) -NH<sub>2</sub>,

(c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

- (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
 (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),  
 (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),  
 (g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,  
 (h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,  
 (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one

triple bond,

- (j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and  
 (k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,

(8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),

(9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two, or three double bonds),

(10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two, or three triple bonds),

(11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(12) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above,

- above,
- (13)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{R}_{1-\text{heteroaryl}}$  where  $\text{R}_{1-\text{heteroaryl}}$  is as defined
- defined above,
- (14)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{R}_{1-\text{heterocycle}}$  where  $\text{R}_{1-\text{heterocycle}}$  is as
- (15)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of:  $\text{C}_1-\text{C}_6$  alkyl,
- (16)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{O}-\text{R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  is selected from the group consisting of:
- (a)  $\text{C}_1-\text{C}_6$  alkyl,
- (b)  $-(\text{CH}_2)_{0-2}-(\text{R}_{1-\text{aryl}})$  where  $\text{R}_{1-\text{aryl}}$  is as defined
- above,
- (c)  $\text{C}_2-\text{C}_6$  alkenyl containing one or two double bonds,
- (d)  $\text{C}_2-\text{C}_6$  alkynyl containing one or two triple bonds,
- (e)  $\text{C}_3-\text{C}_7$  cycloalkyl, and
- (f)  $-(\text{CH}_2)_{0-2}-(\text{R}_{1-\text{heteroaryl}})$  where  $\text{R}_{1-\text{heteroaryl}}$  is as defined above,
- (17)  $-(\text{CH}_2)_{0-4}-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are as defined above,
- (18)  $-(\text{CH}_2)_{0-4}-\text{SO}-(\text{C}_1-\text{C}_8 \text{ alkyl}),$
- (19)  $-(\text{CH}_2)_{0-4}-\text{SO}_2-(\text{C}_1-\text{C}_{12} \text{ alkyl}),$
- (20)  $-(\text{CH}_2)_{0-4}-\text{SO}_2-(\text{C}_3-\text{C}_7 \text{ cycloalkyl}),$
- (21)  $-(\text{CH}_2)_{0-4}-\text{N}(\text{H or } \text{R}_{\text{N-5}})-\text{CO}-\text{O}-\text{R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  can be the same or different and is as defined above,
- (22)  $-(\text{CH}_2)_{0-4}-\text{N}(\text{H or } \text{R}_{\text{N-5}})-\text{CO}-\text{N}(\text{R}_{\text{N-5}})_2,$  where  $\text{R}_{\text{N-5}}$  can be the same or different and is as defined above,

(23)  $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$ , where  $R_{N-5}$  can be the same or different and is as defined above,

(24)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as defined above,

(25)  $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(26)  $-(CH_2)_{0-4}-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(27)  $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(28)  $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$  where  $R_{N-aryl-1}$  is  $-H$  or  $C_1-C_4$  alkyl,

(29)  $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(30)  $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(31)  $-(CH_2)_{0-4}-O-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(32)  $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$  where  $R_{N-5}$  is as defined above,

(33)  $-(CH_2)_{0-4}-S-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(34)  $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, three, four, or five of } -F)$ ,

(35)  $C_3-C_7$  cycloalkyl,

(36)  $C_2-C_6$  alkenyl with one or two double bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(37)  $C_2-C_6$  alkynyl with one or two triple bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, or

(38)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as described above,

(39)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

(C)  $R_{N-aryl}-W-R_{N-aryl}$ ,

(D)  $R_{N-aryl}-W-R_{N-heteroaryl}$ ,

(E)  $R_{N-aryl}-W-R_{N-1-heterocycle}$ , where  $R_{N-1-heterocycle}$  is the same as  $R_1$ .

heterocycle, as defined above,

(F)  $R_{N-heteroaryl}-W-R_{N-aryl}$ ,

(G)  $R_{N-heteroaryl}-W-R_{N-heteroaryl}$ ,

(H)  $R_{N-heteroaryl}-W-R_1-heterocycle$ ,

(I)  $R_1-heterocycle-W-R_{N-aryl}$ ,

(J)  $R_1-heterocycle-W-R_{N-heteroaryl}$ , and

(K)  $R_1-heterocycle-W-R_1-heterocycle$ ,

where W is

(1)  $-(CH_2)_{0-4}-$ ,

(2)  $-O-$ ,

(3)  $-S(O)_{0-2}-$ ,

(4)  $-N(R_{N-5})-$  where  $R_{N-5}$  is as defined above, or

(5)  $-CO-$ ;

(II)  $-CO-(C_1-C_{10} \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A)  $-OH$ ,

(B)  $-C_1-C_6 \text{ alkoxy}$ ,

(C)  $-C_1-C_6 \text{ thioalkoxy}$ ,

(D)  $-CO-O-R_{N-8}$  where  $R_{N-8}$  is  $-H$ ,  $C_1-C_6$  alkyl or  $-phenyl$ ,

(E)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different

and are as defined above,

(F)  $-CO-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(G)  $-SO_2-(C_1-C_8 \text{ alkyl})$ ,

(H)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different

and are as defined above,

(I)  $-NH-CO-(C_1-C_6 \text{ alkyl})$ ,

(J)  $-NH-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,

(K)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and

are as defined above,

- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,
- (N)  $-O-CO-NR_{N-8}R_{N-8}$  where  $R_{N-8}$  are the same or different and are as defined above,
- (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,
- (P)  $-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, or three } -F, -Cl, -Br, \text{ or } -I)$ ,
- (Q)  $-NH-SO_2-(C_1-C_6 \text{ alkyl})$ , and
- (R)  $-F$ , or  $-Cl$ ,
- (III)  $-CO-(C_1-C_6 \text{ alkyl})-O-(C_1-C_6 \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:
- (A)  $-OH$ ,
- (B)  $-C_1-C_6 \text{ alkoxy}$ ,
- (C)  $-C_1-C_6 \text{ thioalkoxy}$ ,
- (D)  $-CO-O-R_{N-8}$  where  $R_{N-8}$  is  $-H$ ,  $C_1-C_6 \text{ alkyl}$  or  $-phenyl$ ,
- (E)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (F)  $-CO-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (G)  $-SO_2-(C_1-C_8 \text{ alkyl})$ ,
- (H)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (I)  $-NH-CO-(C_1-C_6 \text{ alkyl})$ ,
- (J)  $-NH-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,
- (K)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,
- (N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$ s are the same or different and are as defined above,
- (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,

(P)  $-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, or three } -F, -Cl, -Br, \text{ or } -I)_n$

(Q)  $-NH-SO_2-(C_1-C_6 \text{ alkyl})$ , and

(R)  $-F$ , or  $-Cl$ ,

(IV)  $-CO-(C_1-C_6 \text{ alkyl})-S-(C_1-C_6 \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A)  $-OH$ ,

(B)  $-C_1-C_6 \text{ alkoxy}$ ,

(C)  $-C_1-C_6 \text{ thioalkoxy}$ ,

(D)  $-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,

(E)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(F)  $-CO-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(G)  $-SO_2-(C_1-C_8 \text{ alkyl})$ ,

(H)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(I)  $-NH-CO-(C_1-C_6 \text{ alkyl})$ ,

(J)  $-NH-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,

(K)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(N)  $-O-CO-NR_{N-8}R_{N-8}$  where  $R_{N-8}$  are the same or different and are as defined above,

(O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,

(P)  $-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, or three } -F, -Cl, -Br, \text{ or } -I)_n$

(Q)  $-NH-SO_2-(C_1-C_6 \text{ alkyl})$ , and

(R)  $-F$ , or  $-Cl$ ,

(V)  $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-R_{N-aryl}/R_{N-heteroaryl})$  where  $R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above, where  $R_{N-10}$  is selected from the group consisting of:



- (A) -H,
- (B) C<sub>1</sub>-C<sub>6</sub> alkyl,
- (C) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
- (D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,
- (E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,
- (F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and
- (G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above, or

(VI) -CO-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl) where alkyl is optionally substituted with one or two substituents selected from the group consisting of:

- (A) -(CH<sub>2</sub>)<sub>0-4</sub>-OH,
- (B) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (C) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
- (D) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -phenyl,
- (E) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (F) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (G) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (H) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (I) -(CH<sub>2</sub>)<sub>0-4</sub>-NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,
- (K) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (L) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where R<sub>N-8</sub> are the same or different and are as defined above,
- (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(P)  $-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, or three } -F, -Cl, -Br, \text{ or } -I),$

(Q)  $-NH-SO_2-(C_1-C_6 \text{ alkyl}),$  and

(R)  $-F, \text{ or } -Cl;$

where  $R_{N-A}$  is selected from the group consisting of H,  $C_1 - C_{10}$  alkyl,  $C_2 - C_{10}$  alkenyl and alkynyl, phenyl,  $C_1 - C_4$  alkyl- $R_{N-aryl}$ ,  $C_1 - C_4$  alkyl- $R_{N-heteroaryl}$ ,  $C_1 - C_4$  alkyl- $C_3-C_7$  cycloalkyl and  $C_1 - C_4$  alkyl- $R_{1-heterocycle}$ , wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of  $-F, -Cl, -OH, -SH, -C\equiv N, -CF_3, C_1-C_3$  alkoxy,  $-C(O)O-R_{1-a}$ , and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H, C_1-C_6$  alkyl or phenyl;

where Z is selected from the group consisting of:

(A)  $-C(O)-,$

(B)  $-S(O)_{1-2}-,$

(C)  $-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of  $-O-, -S-$  and  $-NR'-$  and where  $R'$  is as defined above; and

(D) a single bond;

where  $R_C$  is:

(I)  $-C_1-C_{10}$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F, -Cl, -Br, -I, -OH, -SH, -C\equiv N, -CF_3, C_1-C_6$  alkoxy,  $-O-phenyl, -NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-OC=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-S(=O)_{0-2} R_{1-a}$  where  $R_{1-a}$  is as defined above,  $-NR_{1-a}C=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-C=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, and  $-S(=O)_2 NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(II)  $-(CH_2)_{0-3}-(C_3-C_8)$  cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F, -Cl, -Br, -I, -OH, -SH, -C\equiv N, -CF_3, C_1-C_6$  alkoxy,  $-O-phenyl, -CO-OH, -CO-O-(C_1-C_4 \text{ alkyl}),$  and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(III)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are

- (A) -H,
- (B)  $\text{C}_1-\text{C}_4$  alkyl optionally substituted with one, or two -OH,
- (C)  $\text{C}_1-\text{C}_4$  alkoxy optionally substituted with one, two, or three -F,
- (D)  $-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7$  cycloalkyl,
- (E)  $\text{C}_2-\text{C}_6$  alkenyl containing one or two double bonds,
- (F)  $\text{C}_2-\text{C}_6$  alkynyl containing one or two triple bonds,
- (G) phenyl-, or
- (A)  $\text{C}_0-\text{C}_4$  alkylC(O)  $\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined

above,

and where  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO<sub>2</sub>-, -NR<sub>N-2</sub>- and  $\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-aryl}}$  is the same as  $\text{R}_{\text{N-aryl}}$  and where  $\text{R}_{\text{C-aryl}}$  may optionally be substituted with  $-\text{C}_0-\text{C}_4$  alkyl-C(O)  $\text{NR}_{1-a}\text{R}_{1-b}$ ,  $\text{C}_0-\text{C}_4$  alkylC(O) OR<sub>1-a</sub> where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(IV)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is the same as  $\text{R}_{\text{N-heteroaryl}}$  and  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(V)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VI)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VII)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VIII)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(IX)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is the same as  $\text{R}_{1-\text{heterocycle}}$ , and where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(X)  $-(\text{R}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XI)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XIII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XIV)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XV)  $-\text{C}(\text{R}_{\text{C-1}})(\text{R}_{\text{C-2}})]_{1-3}-\text{CO}-\text{N}(\text{R}_{\text{C-3}})_2$  where  $\text{R}_{\text{C-3}}$  is as defined below and  $\text{R}_{\text{C-1}}$ ,  $\text{R}_{\text{C-2}}$  are the same or different and are selected from the group consisting of:

(A) -H,

(B)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with up to three substituents independently selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(D)  $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(E)  $\text{C}_2\text{-C}_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(F)  $-(\text{CH}_2)_{1-2}-\text{S}(\text{O})_{0-2}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,

(F)  $-(\text{CH}_2)_{0-4}-\text{C}_3\text{-C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(G)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined for  $\text{R}_{1\text{-aryl}}$ ,

(H)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(I)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

- (J)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,
- (K)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,
- (M)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C'\text{-aryl}}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$  or  $-NR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'\text{-aryl}}$  is defined above,
- (N)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C\text{-heteroaryl}}$  where  $R_{C-4}$  and  $R_{C\text{-heteroaryl}}$  are as defined above, and
- (O)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,
- and where  $R_{C-3}$  is the same or different and is:
- (A)  $-H$ ,
- (B)  $-C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (C)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (D)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (E)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (F)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,
- (G)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,
- (H)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,
- (I)  $-(C_1-C_4 \text{ alkyl})-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,
- (J)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

or

(K)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined

above,

(XVI)  $-\text{CH}(R_{C\text{-aryl}})_2$  where  $R_{C\text{-aryl}}$  are the same or different and are as

defined above,

(XVII)  $-\text{CH}(R_{C\text{-heteroaryl}})_2$  where  $R_{C\text{-heteroaryl}}$  are the same or different and

are as defined above,

(XVIII)  $-\text{CH}(R_{C\text{-aryl}})(R_{C\text{-heteroaryl}})$  where  $R_{C\text{-aryl}}$  and  $R_{C\text{-heteroaryl}}$  are as

defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to  $R_{C\text{-aryl}}$  or

$R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}$  where  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}$  are as defined above

where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with

NH,  $\text{NR}_{N-5}$ , O, or  $\text{S}(=\text{O})_{0-2}$ , and where cyclopentyl, cyclohexyl, or cycloheptyl can be

optionally substituted with one or two  $-C_1-C_3$  alkyl, -F, -OH, -SH,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy, =O, or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XX)  $C_2-C_{10}$  alkenyl containing one or two double bonds optionally

substituted with one, two or three substituents selected from the group consisting of  $C_1-$

$C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy, -O- phenyl, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $C_2-C_{10}$  alkynyl containing one or two triple bonds optionally

substituted with one, two or three substituents selected from the group consisting of  $C_1-$

$C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy, -O- phenyl, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $-(\text{CH}_2)_{0-1}-\text{CHR}_{C-6}-(\text{CH}_2)_{0-1}-R_{C\text{-aryl}}$  where  $R_{C\text{-aryl}}$  is as defined above

and  $R_{C-6}$  is  $-(\text{CH}_2)_{0-6}-\text{OH}$ ,

(XXII)  $-(\text{CH}_2)_{0-1}-\text{CHR}_{C-6}-(\text{CH}_2)_{0-1}-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  and  $R_{C-6}$  is

as defined above,

(XXIII)  $-\text{CH}(-R_{C\text{-aryl}} \text{ or } R_{C\text{-heteroaryl}})-\text{CO}-\text{O}(C_1-C_4 \text{ alkyl})$  where  $R_{C\text{-aryl}}$  and

$R_{C\text{-heteroaryl}}$  are as defined above,

(XXIV)  $-\text{CH}(\text{CH}_2\text{-OH})-\text{CH}(\text{-OH})\text{-phenyl-NO}_2$ ,

(XXV)  $(C_1-C_6 \text{ alkyl})-\text{O}-(C_1-C_6 \text{ alkyl})-\text{OH}$ ,

(XXVII)  $-\text{CH}_2\text{-NH-CH}_2\text{-CH}(\text{-O-CH}_2\text{-CH}_3)_2$ , or

(XXVIII) –  $(\text{CH}_2)_{0-6}\text{-C(=NR}_{1-a})(\text{NR}_{1-a}\text{R}_{1-b})$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

where  $\text{R}_{C-A}$  is H,  $\text{C}_1 - \text{C}_{10}$  alkyl,  $\text{C}_2 - \text{C}_{10}$  alkenyl and alkynyl, phenyl,  $\text{C}_1 - \text{C}_4$  alkyl- $\text{R}_{N\text{-aryl}}$ ,  $\text{C}_1 - \text{C}_4$  alkyl- $\text{R}_{N\text{-heteroaryl}}$ ,  $\text{C}_1 - \text{C}_4$  alkyl- $\text{C}_3\text{-C}_7$  cycloalkyl, or  $\text{C}_1 - \text{C}_4$  alkyl- $\text{R}_{1\text{-heterocycle}}$ , wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $\text{C}_1\text{-C}_3$  alkoxy, -C(O)O- $\text{R}_{1-a}$ , and -NR<sub>1-a</sub>R<sub>1-b</sub> where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are -H,  $\text{C}_1\text{-C}_6$  alkyl or phenyl;

where  $\text{R}_{C-A}$ , -Z- $\text{R}_C$ , and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1)  $\text{C}_1\text{-C}_6$  alkyl,  
 $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, or  
 $\text{C}_2\text{-C}_6$  alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $\text{C}_1\text{-C}_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are -H or  $\text{C}_1\text{-C}_6$  alkyl,

(2) -F, Cl, -Br, or -I,

(3) - $\text{C}_1\text{-C}_6$  alkoxy optionally substituted with one, two, or three -F,

(4) -NR<sub>N-2</sub>R<sub>N-3</sub> where  $\text{R}_{N-2}$  and  $\text{R}_{N-3}$  are as defined below,

(5) -OH,

(6) -C $\equiv$ N,

(7) =O (oxo),

(8) -CO-( $\text{C}_1\text{-C}_4$  alkyl),

(9) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above, or

(10) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

or a pharmaceutically acceptable salt thereof.

16. A disubstituted amine of claim 15, wherein  $R_1$  is:

$-(CH_2)_{0-1}-(R_{1-aryl})$ , or

$-(CH_2)_{n1}-(R_{1-heteroaryl})$ .

17. A disubstituted amine of claim 16, wherein  $R_1$  is:

$-(CH_2)-(R_{1-aryl})$ , or

$-(CH_2)-(R_{1-heteroaryl})$ .

18. A disubstituted amine of claim 17, wherein  $R_1$  is  $-(CH_2)-(R_{1-aryl})$  where  $R_{1-aryl}$  is phenyl.

19. A disubstituted amine of claim 18, wherein  $R_1$  is substituted with two  $-F$ .

20. A disubstituted amine of claim 19, wherein the  $-F$  substitutions are on the -3 and -5 positions.

21. A disubstituted amine of claim 15, wherein  $R_2$  and  $R_3$  are both  $-H$ .

22. A disubstituted amine of claim 15, wherein  $R_C$  is:

$-C_1-C_8$  alkyl,

$-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ , or

-cyclopentyl or -cyclohexyl ring fused to  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

23. A disubstituted amine of claim 22, wherein  $R_C$  is:

$-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,



$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,  
 $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ ,  
 -cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

24. A disubstituted amine of claim 23, wherein  $R_C$  is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,  
 $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,  
 -cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

25. A disubstituted amine of claim 24, wherein  $R_C$  is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-aryl}$  is phenyl.

26. A disubstituted amine of claim 25, wherein said phenyl is substituted in the 3-position or 3,5-positions.

27. A disubstituted amine of claim 15, wherein  $R_{C-A}$  is:

-methyl, or  
 -ethyl.

28. A disubstituted amine of claim 15, wherein Z is:

$-C(O)-$ , or  
 $-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of  $-O-$ ,  $-S-$  and  $-NR'-$ .

29. A disubstituted amine of claim 15, wherein  $R_N$  is:

$-R_{N-1}-X_N-$  where  $X_N$  is  $-CO-$ , where  $R_{N-1}$  is  $R_{N-aryl}$  or  $R_{N-heteroaryl}$  where  $R_{N-aryl}$  is phenyl where the substitution on phenyl is 1,3-, and where  $R_{N-aryl}$  or  $R_{N-heteroaryl}$  are substituted with one  $-CO-NR_{N-2}R_{N-3}$ ,

$-R_{N-1}-X_N-$  where  $X_N$  is  $-CO-$ , where  $R_{N-1}$  is  $R_{N-aryl}$  or  $R_{N-heteroaryl}$  where  $R_{N-aryl}$  is phenyl substituted with one  $C_1$  alkyl where the substitution on the phenyl is 1,3,5-, and where  $R_{N-aryl}$  or  $R_{N-heteroaryl}$  are substituted with one  $-CO-NR_{N-2}R_{N-3}$ , or

$-R_{N-1}-X_N-$  where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N-\text{heteroaryl}}$  where  $R_{N-\text{heteroaryl}}$  is substituted with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$ .

30. A disubstituted amine of claim 29, wherein  $R_{N-2}$  and  $R_{N-3}$  are the same and are  $\text{C}_3$  alkyl.

31. A disubstituted amine of claim 29, wherein  $R_{N-1}-X_N-$  where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N-\text{aryl}}$  where  $R_{N-\text{aryl}}$  is phenyl substituted with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where the substitution on phenyl is 1,3-.

32. A disubstituted amine of claim 29, wherein  $R_{N-1}-X_N-$  where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N-\text{aryl}}$  where  $R_{N-\text{aryl}}$  is phenyl substituted with one  $\text{C}_1$  alkyl and with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where the substitution on the phenyl is 1,3,5-.

33. A disubstituted amine of claim 29, wherein  $X_N$  is  $-\text{CO}-$ , or  $-\text{SO}_2-$ .

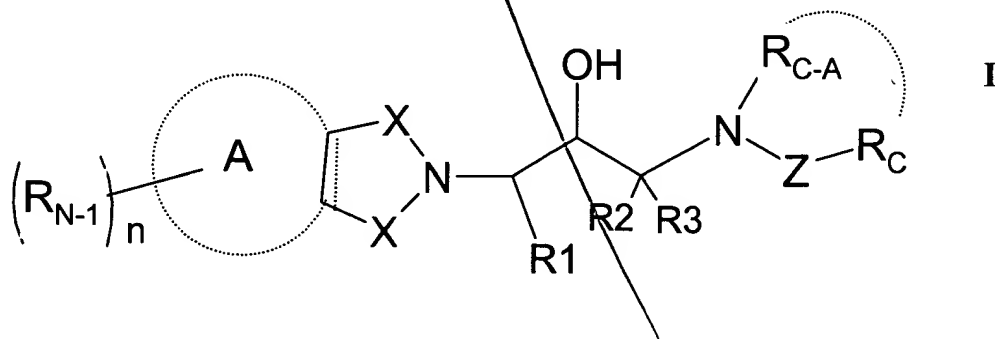
34. A disubstituted amine of claim 29, wherein  $X_N$  is  $-\text{CO}-$ .

35. A compound according to claim 1 or claim 15 selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-({3-  
[(dipropylamino)carbonyl]benzoyl}amino)-2-  
hydroxybutyl](ethylamino)carbonyl}amino)hexanoic acid,  
 $\text{N}^1-((1\text{S},2\text{S})-1-(3,5\text{-difluorobenzyl})-3\text{-}\{\text{ethyl}[(\text{isobutylamino})\text{carbonyl}]\text{amino}\}-2\text{-}$   
 $\text{hydroxypropyl})-\text{N}^3,\text{N}^3\text{-dipropylisophthalamide,}$   
 $\text{N}^1-[(1\text{S},2\text{S})-3\text{-}[(\text{butylsulfonyl})(\text{ethyl})\text{amino}]-1-(3,5\text{-difluorobenzyl})-2\text{-}$   
 $\text{hydroxypropyl}]-5\text{-methyl}-\text{N}^3,\text{N}^3\text{-dipropylisophthalamide,}$   
 $\text{N}^1-((1\text{S},2\text{R})-1-(3,5\text{-difluorobenzyl})-2\text{-hydroxy}-3\text{-}\{(2\text{S})-2\text{-}$   
 $[(\text{isobutylamino})\text{carbonyl}]\text{piperidinyl}\}\text{propyl})-5\text{-methyl}-\text{N}^3,\text{N}^3\text{-dipropylisophthalamide,}$   
 $\text{N}^1-[(1\text{S},2\text{R})-1-(3,5\text{-difluorobenzyl})-2\text{-hydroxy}-3\text{-}(4\text{-methyl}-1\text{-}$   
 $\text{piperazinyl})\text{propyl}]-5\text{-methyl}-\text{N}^3,\text{N}^3\text{-dipropylisophthalamide,}$

$N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[2-(isobutylamino)-2-oxoethyl](methylamino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl](methylamino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]- $N^3,N^3$ -dipropylisophthalamide, and  
 $N^1$ -{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide.

36. A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of a disubstituted amine of formula (I)



where  $R_1$  is:

(I)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $C_1-C_7$  alkyl (optionally substituted with  $C_1-C_3$  alkyl and  $C_1-C_3$  alkoxy),  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl, and  $-OC=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(II)  $-CH_2-S(O)_{0-2}-(C_1-C_6 \text{ alkyl})$ ,

(III)  $-CH_2-CH_2-S(O)_{0-2}-(C_1-C_6 \text{ alkyl})$ ,

(IV)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

(V)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

(VI)  $-(CH_2)_{n1}-(R_{1-aryl})$  where  $n_1$  is zero or one and where  $R_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A)  $C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(B)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

(C)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

(D)  $-F$ ,  $Cl$ ,  $-Br$  or  $-I$ ,

(F)  $-C_1-C_6$  alkoxy optionally substituted with one, two, or three  $-F$ ,

(G)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined below,

(H) -OH,

(I) -C≡N,

(J) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(K) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(L) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(M) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(N) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heteroaryl</sub>) where n<sub>1</sub> is as defined above and where R<sub>1-</sub>

heteroaryl is selected from the group consisting of:

pyridinyl,

pyrimidinyl,

quinolinyl,

benzothienyl,

indolyl,

indolinyl,

pyridazinyl,

pyrazinyl,

isoquinolyl,

quinazolinyl,

quinoxalinyl,

phthalazinyl,

imidazolyl,

isoxazolyl,

pyrazolyl,

oxazolyl,

thiazolyl,

indolizinyl,

indazolyl,

benzothiazolyl,

benzimidazolyl,  
benzofuranyl,  
furanyl,  
thienyl,  
pyrrolyl,  
oxadiazolyl,  
thiadiazolyl,  
triazolyl,  
tetrazolyl,  
oxazolopyridinyl,  
imidazopyridinyl,  
isothiazolyl,  
naphthyridinyl,  
cinnolinyl,  
carbazolyl,  
beta-carbolinyl,  
isochromanyl,  
chromanyl,  
tetrahydroisoquinolinyl,  
isoindolinyl,  
isobenzotetrahydrofuranyl,  
isobenzotetrahydrothienyl,  
isobenzothienyl,  
benzoxazolyl,  
pyridopyridinyl,  
benzotetrahydrofuranyl,  
benzotetrahydrothienyl,  
purinyl,  
benzodioxolyl,  
triazinyl,  
phenoxazinyl,

phenothiazinyl,  
pteridinyl,  
benzothiazolyl,  
imidazopyridinyl,  
imidazothiazolyl,  
dihydrobenzisoaxazinyl,  
benzisoaxazinyl,  
benzoxazinyl,  
dihydrobenzisothiazinyl,  
benzopyranyl,  
benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromonyl,  
chromanonyl,  
pyridinyl-N-oxide,  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisoquinolinonyl  
dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,

indoliny N-oxide,  
 isoquinolyl N-oxide,  
 quinazolinyl N-oxide,  
 quinoxaliny N-oxide,  
 phthalazinyl N-oxide,  
 imidazolyl N-oxide,  
 isoxazolyl N-oxide,  
 oxazolyl N-oxide,  
 thiazolyl N-oxide,  
 indoliziny N-oxide,  
 indazolyl N-oxide,  
 benzothiazolyl N-oxide,  
 benzimidazolyl N-oxide,  
 pyrrolyl N-oxide,  
 oxadiazolyl N-oxide,  
 thiadiazolyl N-oxide,  
 triazolyl N-oxide,  
 tetrazolyl N-oxide,  
 benzothiopyranyl S-oxide, and  
 benzothiopyranyl S,S-dioxide,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{n1}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four:

(1)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(2)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,



(3) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(4) -F, Cl, -BR, or -I,

(6) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(8) -OH,

(9) -C≡N,

(10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), with the proviso that when n<sub>1</sub> is zero R<sub>1-</sub>

heteroaryl is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heterocycle</sub>) where n<sub>1</sub> is as defined above and R<sub>1-heterocycle</sub> is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

pyrrolidinyl,

pyrrolinyl,

tetrahydropyranyl,

piperidinyl,

tetrahydrofuranyl,

tetrahydrothienyl,

homopiperidinyl,  
 homomorpholinyl,  
 homothiomorpholinyl,  
 homothiomorpholinyl S,S-dioxide,  
 oxazolidinonyl,  
 dihydropyrazolyl,  
 dihydropyrrolyl,  
 dihydropyrazinyl,  
 dihydropyridinyl,  
 dihydropyrimidinyl,  
 dihydrofuryl,  
 dihydropyranyl,  
 tetrahydrothienyl S-oxide,  
 tetrahydrothienyl S,S-dioxide, and  
 homothiomorpholinyl S-oxide,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heterocycle}}$  group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1)  $C_1\text{-}C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1\text{-}C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2)  $C_2\text{-}C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(3)  $C_2\text{-}C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(4) -F, Cl, -Br, or -I,

- (5) C<sub>1</sub>-C<sub>6</sub> alkoxy,  
 (6) -C<sub>1</sub>-C<sub>6</sub> alkoxy substituted with one, two, or three -F,  
 (7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,  
 (8) -OH,  
 (9) -C≡N,  
 (10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,  
 (11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),  
 (12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,  
 (13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,  
 (14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), or  
 (15) =O, with the proviso that when n<sub>1</sub> is zero R<sub>1-heterocycle</sub> is not bonded to the carbon chain by nitrogen;

where R<sub>2</sub> is:

- (I)-H,  
 (II) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,  
 (III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub> where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above;  
 (IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,  
 (V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, or

(VI)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl,

where  $R_3$  is:

(I)  $-H$ ,

(II)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(III)  $-(CH_2)_{0-4}-R_{2-1}$  where  $R_{2-1}$  is  $R_{1-aryl}$  or  $R_{1-heteroaryl}$  where  $R_{1-aryl}$  and  $R_{1-heteroaryl}$  are as defined above;

(IV)  $C_2-C_6$  alkenyl with one or two double bonds,

(V)  $C_2-C_6$  alkynyl with one or two triple bonds, or

(VI)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1-C_6$  alkyl, where  $R_2$  and  $R_3$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-SO_2-$ , and  $-NR_{N-2}-$ ,

where  $R_{N-2}$  is selected from the group consisting of:

(a)  $-H$ ,

(b)  $C_1-C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:

(i)  $-OH$ , and

(ii)  $-NH_2$ ,

(c)  $C_1-C_6$  alkyl optionally substituted with one to three  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,

(d)  $C_3-C_7$  cycloalkyl,

(e)  $-(C_1-C_2 \text{ alkyl})-(C_3-C_7 \text{ cycloalkyl})$ ,

(f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,

- triple bond,
- (g)  $-C_2-C_6$  alkenyl with one or two double bonds,
  - (h)  $-C_2-C_6$  alkynyl with one or two triple bonds,
  - (i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,
  - (j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, and
  - (k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above;

where X is independently chosen from the group consisting of:

- $-C(O)-$ ,
- $-CH_2-$ ,
- $-CH_2-CH_2-$ , and
- $-CH_2-C(O)-$ ;

wherein in the rings drawn, a dotted line indicates an optional double bond or an optional ring;

wherein ring A is phenyl, cyclohexyl, cyclopentyl, pyridyl, pyrimidinyl, pyrazinyl or is absent; and

where  $R_{N-1}$  is selected from the group consisting of:

- (1)  $C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

- (2)  $-OH$ ,
- (3)  $-NO_2$ ,
- (4)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (5)  $-CO-OH$ ,
- (6)  $-C\equiv N$ ,

(7)  $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are selected from the group consisting of:

- (a)  $-H$ ,
- (b)  $-C_1-C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:

- (i) -OH, and  
(ii) -NH<sub>2</sub>,  
(c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,  
(d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
(e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),  
(f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),  
(g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,  
(h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,  
(i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,  
(j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and  
(k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,  
(8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),  
(9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two, or three double bonds),  
(10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two, or three triple bonds),  
(11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),  
(12) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above,  
(13) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,  
(14) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as defined above,  
(15) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homoythiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of: C<sub>1</sub>-C<sub>6</sub> alkyl,  
(16) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is selected from the group consisting of:

- above,  
bonds,  
bonds,  
defined above,  
defined above,
- (a) C<sub>1</sub>-C<sub>6</sub> alkyl,  
(b) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-aryl</sub>) where R<sub>1-aryl</sub> is as defined  
(c) C<sub>2</sub>-C<sub>6</sub> alkenyl containing one, or two double  
(d) C<sub>2</sub>-C<sub>6</sub> alkynyl containing one, or two triple  
(e) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and  
(f) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-heteroaryl</sub>) where R<sub>1-heteroaryl</sub> is as  
defined above,
- (17) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as  
defined above,
- (18) -(CH<sub>2</sub>)<sub>0-4</sub>-SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),  
(19) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>12</sub> alkyl),  
(20) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),  
(21) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> can be  
the same or different and is as defined above,  
(22) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub> can  
be the same or different and is as defined above,  
(23) -(CH<sub>2</sub>)<sub>0-4</sub>-N-CS-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub> can be the same  
or different and is as defined above,  
(24) -(CH<sub>2</sub>)<sub>0-4</sub>-N(-H or R<sub>N-5</sub>)-CO-R<sub>N-2</sub> where R<sub>N-5</sub> and R<sub>N-2</sub>  
can be the same or different and are as defined above,  
(25) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the  
same or different and are as defined above,  
(26) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,  
(27) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
(28) -(CH<sub>2</sub>)<sub>0-4</sub>-O-P(O)-(OR<sub>N-aryl-1</sub>)<sub>2</sub> where R<sub>N-aryl-1</sub> is -H or  
C<sub>1</sub>-C<sub>4</sub> alkyl,  
above,
- (29) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-N(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined

above,

(30)  $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined

(31)  $-(CH_2)_{0-4}-O-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(32)  $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$  where  $R_{N-5}$  is as defined

above,

(33)  $-(CH_2)_{0-4}-S-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(34)  $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, three, four, or five of: } -F),$

(35)  $C_3-C_7$  cycloalkyl,

(36)  $C_2-C_6$  alkenyl with one or two double bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(37)  $C_2-C_6$  alkynyl with one or two triple bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(38)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as described above, and

(39)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl;

where  $n$  is equal to 0, 1, 2 or 3;

where  $Z$  is selected from the group consisting of:

(A)  $-C(O)-$ ,

(B)  $-S(O)_{1-2}-$ ,

(C)  $-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of  $-O-$ ,  $-S-$  and  $-NR'$  and where  $R'$  is as defined above; and

(D) a single bond;

where  $R_C$  is:

(I)  $C_1-C_{10}$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,



-SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O-phenyl, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, -OC=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, -S(=O)<sub>0-2</sub> R<sub>1-a</sub> where R<sub>1-a</sub> is as defined above, -NR<sub>1-a</sub>C=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, -C=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, and -S(=O)<sub>2</sub> NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>8</sub>) cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O-phenyl, -CO-OH, -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl), and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(III) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are

(I) -H,

(J) C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with one or two -OH,,

(K) C<sub>1</sub>-C<sub>4</sub> alkoxy optionally substituted with one, two, or three -F,

(L) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(M) C<sub>2</sub>-C<sub>6</sub> alkenyl containing one or two double bonds,

(N) C<sub>2</sub>-C<sub>6</sub> alkynyl containing one or two triple bonds,

(O) phenyl-,

(P) C<sub>0</sub>-C<sub>4</sub> alkylC(O) NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined

above,

and where R<sub>C-x</sub> and R<sub>C-y</sub> are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO<sub>2</sub>-, -NR<sub>N-2</sub>- and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub> and where R<sub>C-aryl</sub> may optionally be substituted with -C<sub>0</sub>-C<sub>4</sub> alkyl-C(O) NR<sub>1-a</sub>R<sub>1-b</sub>, C<sub>0</sub>-C<sub>4</sub> alkylC(O) OR<sub>1-a</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(IV) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is the same as R<sub>N-heteroaryl</sub> and R<sub>C-x</sub> and R<sub>C-y</sub> are as defined above,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub>-R<sub>C-aryl</sub> where R<sub>C-aryl</sub>, R<sub>C-x</sub> and R<sub>C-y</sub> are as defined above,

(VI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$  where  $R_{C-aryl}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(IX)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-}$  heterocycle, and  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(X)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$  where  $R_{C-heteroaryl}$ ,  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIV)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$ , and  $R_{C-y}$  are as defined above,

(XV)  $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$  where  $R_{C-3}$  is as defined below and  $R_{C-1}$ ,  $R_{C-2}$  are the same or different and are selected from the group consisting of:

(A) -H,

(B)  $-C_1-C_6$  alkyl, optionally substituted with one, two, or three substituents independently selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(D)  $C_2-C_6$  alkenyl with one, or two double bonds, optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(E)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1-$

C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(F) -(CH<sub>2</sub>)<sub>1-2</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(F) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(G) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined for R<sub>1-aryl</sub>,

(H) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(I) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(J) -R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(K) -R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(M) -(CH<sub>2</sub>)<sub>1-4</sub>-R<sub>C-4</sub>-(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C'-aryl</sub> where R<sub>C-4</sub> is -O-, -S- or -NR<sub>C-5</sub>- where R<sub>C-5</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, and where R<sub>C'-aryl</sub> is defined above,

(N) -(CH<sub>2</sub>)<sub>1-4</sub>-R<sub>C-4</sub>-(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-4</sub> and R<sub>C-heteroaryl</sub> are as defined above, and

(O) -R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined above,

and where R<sub>C-3</sub> is the same or different and is:

(a) -H,

(b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(c) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(d) C<sub>2</sub>-C<sub>6</sub> alkynyl with one, or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-

C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(e) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(f) -R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined above,

(g) -R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(h) -R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(i) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C'-aryl</sub> where R<sub>C'-aryl</sub> is as defined above,

(j) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is as defined above,

(k) -(C<sub>1</sub>-C<sub>4</sub> alkyl)-R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub> is as defined above,

(XVI) -CH(R<sub>C-aryl</sub>)<sub>2</sub> where R<sub>C-aryl</sub> are the same or different and are as defined above,

(XVII) -CH(R<sub>C-heteroaryl</sub>)<sub>2</sub> where R<sub>C-heteroaryl</sub> are the same or different and are as defined above,

(XVIII) -CH(R<sub>C-aryl</sub>)(R<sub>C-heteroaryl</sub>) where R<sub>C-aryl</sub> and R<sub>C-heteroaryl</sub> are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to R<sub>C-aryl</sub> or R<sub>C-heteroaryl</sub> or R<sub>C-heterocycle</sub> where R<sub>C-aryl</sub> or R<sub>C-heteroaryl</sub> or R<sub>C-heterocycle</sub> are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH, NR<sub>N-5</sub>, O, or S(=O)<sub>0-2</sub>, and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one, or two -C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, =O, or -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(XX) C<sub>2</sub>-C<sub>10</sub> alkenyl containing one or two double bonds optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(XXI) C<sub>2</sub>-C<sub>10</sub> alkynyl containing one, or two triple bonds optionally substituted with one, two, or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O- phenyl, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(XXI) -(CH<sub>2</sub>)<sub>0-1</sub>-CHR<sub>C-6</sub>-(CH<sub>2</sub>)<sub>0-1</sub>-R<sub>C-aryl</sub> where R<sub>C-aryl</sub> is as defined above and R<sub>C-6</sub> is -(CH<sub>2</sub>)<sub>0-6</sub>-OH,

(XXII) -(CH<sub>2</sub>)<sub>0-1</sub>-CHR<sub>C-6</sub>-(CH<sub>2</sub>)<sub>0-1</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> and R<sub>C-6</sub> is as defined above,

(XXIII) -CH(-R<sub>C-aryl</sub> or R<sub>C-heteroaryl</sub>)-CO-O(C<sub>1</sub>-C<sub>4</sub> alkyl) where R<sub>C-aryl</sub> and R<sub>C-heteroaryl</sub> are as defined above,

(XXIV) -CH(-CH<sub>2</sub>-OH)-CH(-OH)-phenyl-NO<sub>2</sub>,

(XXV) (C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>6</sub> alkyl)-OH,

(XXVII) -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH(-O-CH<sub>2</sub>-CH<sub>3</sub>)<sub>2</sub>, or

(XXVIII) -(CH<sub>2</sub>)<sub>0-6</sub>-C(=NR<sub>1-a</sub>)(NR<sub>1-a</sub>R<sub>1-b</sub>) where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

where R<sub>C-A</sub> is H, C<sub>1</sub> - C<sub>10</sub> alkyl, C<sub>2</sub> - C<sub>10</sub> alkenyl and alkynyl, phenyl, C<sub>1</sub> - C<sub>4</sub> alkyl-R<sub>N-aryl</sub>, C<sub>1</sub> - C<sub>4</sub> alkyl-R<sub>N-heteroaryl</sub>, C<sub>1</sub> - C<sub>4</sub> alkyl-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or C<sub>1</sub> - C<sub>4</sub> alkyl-R<sub>1-heterocycle</sub>, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -C(O)O-R<sub>1-a</sub>, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H, C<sub>1</sub>-C<sub>6</sub> alkyl or phenyl;

where R<sub>C-A</sub>, -Z-R<sub>C</sub>, and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1) C<sub>1</sub>-C<sub>6</sub> alkyl,

C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, or

C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(8) -F, Cl, -Br, or -I,

(10) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(11) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(12) -OH,

(13) -C≡N,

(14) =O (oxo),

(15) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(16) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(10)-CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above;

or a pharmaceutically acceptable salt thereof.

37. A method of treatment according to claim 36, wherein the disease is Alzheimer's disease.

38. A method of treatment according to claim 36, wherein the method is helping prevent or delay the onset of Alzheimer's disease.

39. A method of treatment according to claim 36, wherein the disease is mild cognitive impairment.

40. A method of treatment according to claim 36, wherein the disease is Down's syndrome.

41. A method of treatment according to claim 36, wherein the disease is Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type.

42. A method of treatment according to claim 36, wherein the disease is cerebral amyloid angiopathy.
43. A method of treatment according to claim 36, wherein the disease is degenerative dementias.
44. A method of treatment according to claim 36, wherein the disease is diffuse Lewy body type of Alzheimer's disease.
45. A method of treatment according to claim 36, wherein the method is treating an existing disease.
46. A method of treatment according to claim 36, wherein the method is preventing a disease from developing.
47. A method of treatment according to claim 36, wherein the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.
48. A method of treatment according to claim 47, wherein the therapeutically effective amount for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.
49. A method of treatment according to claim 48 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.
50. A method of treatment according to claim 36, wherein  $R_1$  is:  
 $-(CH_2)_{0-1}-(R_{1-aryl})$ , or

$-(CH_2)_{n1}-(R_{1\text{-heteroaryl}}).$

51. A method of treatment according to claim 50, wherein  $R_1$  is:

$-(CH_2)-(R_{1\text{-aryl}}),$  or

$-(CH_2)-(R_{1\text{-heteroaryl}}).$

52. A method of treatment according to claim 51, wherein  $R_1$  is  $-(CH_2)-(R_{1\text{-aryl}})$  where  $R_{1\text{-aryl}}$  is phenyl.

53. A method of treatment according to claim 52, wherein  $R_1$  is substituted with two  $-F$ .

54. A method of treatment according to claim 53, wherein the  $-F$  substitutions are on the -3 and -5 positions.

55. A method of treatment according to claim 36, wherein  $R_2$  and  $R_3$  are both  $-H$ .

56. A method of treatment according to claim 36, wherein  $R_C$  is:

$-C_1-C_8$  alkyl,

$-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-aryl}},$

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-heteroaryl}},$

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-heterocycle}},$  or

-cyclopentyl or -cyclohexyl ring fused to  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}.$

57. A method of treatment according to claim 56, wherein  $R_C$  is:

$-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-aryl}},$

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-heteroaryl}},$

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-heterocycle}},$  or

-cyclopentyl or -cyclohexyl ring fused to a  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}.$



58. A method of treatment according to claim 57, wherein  $R_C$  is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ ,

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ ,

-cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

59. A method of treatment according to claim 58, wherein  $R_C$  is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-aryl}$  is phenyl.

60. A method of treatment according to claim 59, wherein said phenyl is substituted in the 3-position or 3,5-positions.

61. A method of treatment according to claim 36, wherein  $R_{C-A}$  is:

-methyl, or

-ethyl.

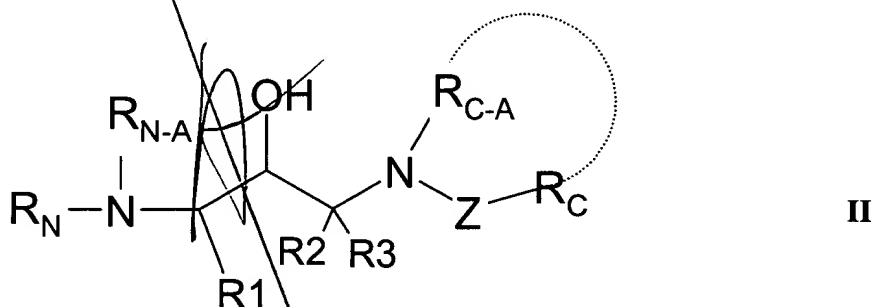
62. A method of treatment according to claim 36, wherein  $Z$  is:

$-C(O)-$ , or

$-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of  $-O-$ ,  $-S-$  and  $-NR'-$ .

63. A method of treatment according to claim 36 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids: acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

64. A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of a disubstituted amine of formula II



where  $R_1$  is:

(I)  $C_1$ - $C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl,  $C_1$ - $C_7$  alkyl (optionally substituted with  $C_1$ - $C_3$  alkyl and  $C_1$ - $C_3$  alkoxy),  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  $-H$  or  $C_1$ - $C_6$  alkyl, and  $-OC=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(II)  $-CH_2-S(O)_{0-2}-(C_1-C_6 \text{ alkyl})$ ,

(III)  $-CH_2-CH_2-S(O)_{0-2}-(C_1-C_6 \text{ alkyl})$ ,

(IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(VI) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-aryl</sub>) where n<sub>1</sub> is zero or one and where R<sub>1-aryl</sub> is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(B) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(D) -F, Cl, -Br or -I,

(F) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(G) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(H) -OH,

(I) -C≡N,

(J) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(K) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(L) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(M) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, or

(N) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1</sub>-heteroaryl) where n<sub>1</sub> is as defined above and where R<sub>1</sub>.

heteroaryl is selected from the group consisting of:

pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoquinolyl,  
quinazolinyl,  
quinoxalinyl,  
phthalazinyl,  
imidazolyl,  
isoxazolyl,  
pyrazolyl,  
oxazolyl,  
thiazolyl,  
indolizinyl,  
indazolyl,  
benzothiazolyl,  
benzimidazolyl,  
benzofuranyl,  
furanyl,  
thienyl,  
pyrrolyl,  
oxadiazolyl,  
thiadiazolyl,  
triazolyl,

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tetrazolyl,  
oxazolopyridinyl,  
imidazopyridinyl,  
isothiazolyl,  
naphthyridinyl,  
cinnolinyl,  
carbazolyl,  
beta-carbolinyl,  
isochromanlyl,  
chromanlyl,  
tetrahydroisoquinolinyl,  
isoindolinyl,  
isobenzotetrahydrofuranyl,  
isobenzotetrahydrothienyl,  
isobenzothienyl,  
benzoxazolyl,  
pyridopyridinyl,  
benzotetrahydrofuranyl,  
benzotetrahydrothienyl,  
purinyl,  
benzodioxolyl,  
triazinyl,  
phenoxazinyl,  
phenothiazinyl,  
pteridinyl,  
benzothiazolyl,  
imidazopyridinyl,  
imidazothiazolyl,  
dihydrobenzisoxazinyl,  
benzisoxazinyl,  
benzoxazinyl,

dihydrobenzothiazinyl,  
benzopyranyl,  
benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromonyl,  
chromanonyl,  
pyridinyl-N-oxide,  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisoquinolinonyl  
dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,  
indolinyl N-oxide,  
isoquinolyl N-oxide,  
quinazolinyl N-oxide,  
quinoxalinyl N-oxide,  
phthalazinyl N-oxide,  
imidazolyl N-oxide,  
isoxazolyl N-oxide,  
oxazolyl N-oxide,

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thiazolyl N-oxide,  
 indoliziny N-oxide,  
 indazolyl N-oxide,  
 benzothiazolyl N-oxide,  
 benzimidazolyl N-oxide,  
 pyrrolyl N-oxide,  
 oxadiazolyl N-oxide,  
 thiadiazolyl N-oxide,  
 triazolyl N-oxide,  
 tetrazolyl N-oxide,  
 benzothiopyranyl S-oxide, and  
 benzothiopyranyl S,S-dioxide,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{n1}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four:

- (1)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,
- (2)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,
- (3)  $C_2$ - $C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1$ - $C_6$  alkyl,
- (4) -F, Cl, -BR, or -I,
- (6)  $-C_1$ - $C_6$  alkoxy optionally substituted with one, two, or three -F,
- (7)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined below,
- (8) -OH,

(9)  $-\text{C}\equiv\text{N}$ ,

(10)  $\text{C}_3\text{-C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1\text{-C}_6$  alkyl,

(11)  $-\text{CO}-(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,

(12)  $-\text{SO}_2\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(13)  $-\text{CO}\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above, or

(14)  $-\text{SO}_2-(\text{C}_1\text{-C}_4 \text{ alkyl})$ , with the proviso that when  $n_1$  is zero  $\text{R}_{1-}$

heteroaryl is not bonded to the carbon chain by nitrogen, or

(VIII)  $-(\text{CH}_2)_{n_1}\text{-(R}_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and  $\text{R}_{1\text{-heterocycle}}$  is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

pyrrolidinyl,

pyrrolinyl,

tetrahydropyranyl,

piperidinyl,

tetrahydrofuranyl,

tetrahydrothienyl,

homopiperidinyl,

homomorpholinyl,

homothiomorpholinyl,

homothiomorpholinyl S,S-dioxide,

oxazolidinonyl,

dihydropyrazolyl,

dihydropyrrolyl,

dihydropyrazinyl,



dihydropyridinyl,  
 dihydropyrimidinyl,  
 dihydrofuryl,  
 dihydropyranyl,  
 tetrahydrothienyl S-oxide,  
 tetrahydrothienyl S,S-dioxide, and  
 homothiomorpholinyl S-oxide,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heterocycle}}$  group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1)  $C_1\text{-}C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1\text{-}C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2)  $C_2\text{-}C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(3)  $C_2\text{-}C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(4) -F, Cl, -Br, or -I,

(5)  $C_1\text{-}C_6$  alkoxy,

(6)  $C_1\text{-}C_6$  alkoxy substituted with one, two, or three -F,

(7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(8) -OH,

(9) -C $\equiv$ N,

(10)  $C_3\text{-}C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C $\equiv$ N, -CF<sub>3</sub>,  $C_1\text{-}C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or  $C_1\text{-}C_6$  alkyl,

(11)  $-\text{CO}-(\text{C}_1\text{-C}_4 \text{ alkyl}),$

(12)  $-\text{SO}_2\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined

above,

(13)  $-\text{CO-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined

above,

(14)  $-\text{SO}_2-(\text{C}_1\text{-C}_4 \text{ alkyl}),$  or

(15)  $=\text{O}$ , with the proviso that when  $n_1$  is zero  $\text{R}_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $\text{R}_2$  is:

(I)-H,

(II)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(III)  $-(\text{CH}_2)_{0-4}\text{-R}_{2-1}$  where  $\text{R}_{2-1}$  is  $\text{R}_{1\text{-aryl}}$  or  $\text{R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-aryl}}$  and  $\text{R}_{1\text{-heteroaryl}}$  are as defined above;

(IV)  $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1\text{-C}_6$  alkyl,

(V)  $\text{C}_2\text{-C}_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1\text{-C}_6$  alkyl, or

(VI)  $-(\text{CH}_2)_{0-4}\text{-C}_3\text{-C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  $-\text{H}$  or  $\text{C}_1\text{-C}_6$  alkyl,

where  $\text{R}_3$  is selected from the group consisting of:

(I)-H,

(II)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(III)  $-(CH_2)_{0-4}-R_{2-1}$  where  $R_{2-1}$  is  $R_{1-aryl}$  or  $R_{1-heteroaryl}$  where  $R_{1-aryl}$  and  $R_{1-heteroaryl}$  are as defined above;

(IV)  $C_2-C_6$  alkenyl with one or two double bonds,

(V)  $C_2-C_6$  alkynyl with one or two triple bonds, or

(VI)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1-C_6$  alkyl,

and where  $R_2$  and  $R_3$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-,  $-SO_2-$ , and  $-NR_{N-2}-$ ,

where  $R_{N-2}$  is selected from the group consisting of:

- (a) -H,
- (b)  $C_1-C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:
  - (i) -OH, and
  - (ii)  $-NH_2$ ,
- (c)  $C_1-C_6$  alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
- (d)  $C_3-C_7$  cycloalkyl,
- (e)  $-(C_1-C_2 \text{ alkyl})-(C_3-C_7 \text{ cycloalkyl})$ ,
- (f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,
- (g)  $C_2-C_6$  alkenyl with one or two double bonds,
- (h)  $C_2-C_6$  alkynyl with one or two triple bonds,
- (i)  $C_1-C_6$  alkyl chain with one double bond and one triple bond,
- (j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, and
- (k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above;

where  $R_N$  is:

(I)  $R_{N-1}-X_N$  where  $X_N$  is selected from the group consisting of:

- (A)  $-\text{CO}-$ ,
- (B)  $-\text{SO}_2-$ ,
- (C)  $-(\text{CR}'\text{R}'')_{1-6}$  where  $\text{R}'$  and  $\text{R}''$  are the same or different and are  $-\text{H}$  or  $\text{C}_1\text{-C}_4$  alkyl,
- (D)  $-\text{CO}-(\text{CR}'\text{R}'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is selected from the group consisting of  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'-$  and where  $\text{R}'$  and  $\text{R}''$  are as defined above, and
- (E) a single bond;

where  $R_{N-1}$  is selected from the group consisting of:

(A)  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, or dihydronaphthyl optionally substituted with one, two or three of the following substituents which can be the same or different and are:

(1)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

- (2)  $-\text{OH}$ ,
- (3)  $-\text{NO}_2$ ,
- (4)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,
- (5)  $-\text{CO}-\text{OH}$ ,
- (6)  $-\text{C}\equiv\text{N}$ ,

(7)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where  $\text{R}_{N-2}$  and  $\text{R}_{N-3}$  are the same or different and are selected from the group consisting of:

- (a)  $-\text{H}$ ,
- (b)  $\text{C}_1\text{-C}_6$  alkyl optionally substituted with one substituent selected from the group consisting of:
  - (i)  $-\text{OH}$ , and
  - (ii)  $-\text{NH}_2$ ,

three -F, -Cl, -Br, or -I,

(c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to

(d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),

(g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,

(i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one

triple bond,

(j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and

(k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,

(8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),

(9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two or three

double bonds),

(10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two or three

triple bonds),

(11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(12) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above,

(13) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined

above,

(14) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as

defined above,

(15) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is selected from the

group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl,

homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide,

homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is

optionally substituted with one, two, three, or four of: C<sub>1</sub>-C<sub>6</sub> alkyl,

(16) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is selected from the group

consisting of:

(a) C<sub>1</sub>-C<sub>6</sub> alkyl,

- above,
- (b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined
- bonds,
- (c)  $C_2-C_6$  alkenyl containing one or two double
- bonds,
- (d)  $C_2-C_6$  alkynyl containing one or two triple
- (e)  $C_3-C_7$  cycloalkyl,
- (f)  $-(CH_2)_{0-2}-(R_{1-heteroaryl})$  where  $R_{1-heteroaryl}$  is as
- defined above,
- (17)  $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as
- defined above,
- (18)  $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$ ,
- (19)  $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$ ,
- (20)  $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$ ,
- (21)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$  where  $R_{N-5}$  can be
- the same or different and is as defined above,
- (22)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$ , where  $R_{N-5}$  can
- be the same or different and is as defined above,
- (23)  $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$ , where  $R_{N-5}$  can be the same
- or different and is as defined above,
- (24)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$
- can be the same or different and are as defined above,
- (25)  $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the
- same or different and are as defined above,
- (26)  $-(CH_2)_{0-4}-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (27)  $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$ ,
- (28)  $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$  where  $R_{N-aryl-1}$  is  $-H$  or
- $C_1-C_4$  alkyl,
- (29)  $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined
- above,

above,

(30)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{CS}-\text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined

(31)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(32)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2-\text{COOH}$  where  $\text{R}_{\text{N}-5}$  is as defined

above,

(33)  $-(\text{CH}_2)_{0-4}-\text{S}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(34)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl optionally substituted with one, two, three, four, or five } -\text{F}),$

(35)  $\text{C}_3-\text{C}_7$  cycloalkyl,

(36)  $\text{C}_2-\text{C}_6$  alkenyl with one or two double bonds optionally substituted with  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_3$  alkoxy, or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(37)  $\text{C}_2-\text{C}_6$  alkynyl with one or two triple bonds optionally substituted with  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_3$  alkoxy, or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(38)  $-(\text{CH}_2)_{0-4}-\text{N}(-\text{H or } \text{R}_{\text{N}-5})-\text{SO}_2-\text{R}_{\text{N}-2}$  where  $\text{R}_{\text{N}-5}$  and  $\text{R}_{\text{N}-2}$  can be the same or different and are as described above, or

(39)  $-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7$  cycloalkyl,

(B)  $-\text{R}_{\text{N-heteroaryl}}$ , where  $\text{R}_{\text{N-heteroaryl}}$  is selected from the group as defined above in  $\text{R}_{1-\text{heteroaryl}}$  and where the  $\text{R}_{\text{N-heteroaryl}}$  group is bonded by any atom of the parent  $\text{R}_{\text{N-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $\text{R}_{\text{N-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1)  $\text{C}_1-\text{C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(2)  $-\text{OH}$ ,

(3)  $-\text{NO}_2$ ,

(4)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

(5)  $-\text{CO}-\text{OH}$ ,

(6)  $-C\equiv N$ ,

(7)  $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are selected from the group consisting of:

(a)  $-H$ ,

(b)  $-C_1-C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:

(i)  $-OH$ , and

(ii)  $-NH_2$ ,

(c)  $-C_1-C_6$  alkyl optionally substituted with one to three  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,

(d)  $-C_3-C_7$  cycloalkyl,

(e)  $-(C_1-C_2 \text{ alkyl})-(C_3-C_7 \text{ cycloalkyl})$ ,

(f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,

(g)  $-C_2-C_6$  alkenyl with one or two double bonds,

(h)  $-C_2-C_6$  alkynyl with one or two triple bonds,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, and

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(8)  $-(CH_2)_{0-4}-CO-(C_1-C_{12} \text{ alkyl})$ ,

(9)  $-(CH_2)_{0-4}-CO-(C_2-C_{12} \text{ alkenyl with one, two, or three double bonds})$ ,

(10)  $-(CH_2)_{0-4}-CO-(C_2-C_{12} \text{ alkynyl with one, two, or three triple bonds})$ ,

(11)  $-(CH_2)_{0-4}-CO-(C_3-C_7 \text{ cycloalkyl})$ ,

(12)  $-(CH_2)_{0-4}-CO-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,

(13)  $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(14)  $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,



(15)  $-(CH_2)_{0-4}-CO-R_{N-4}$  where  $R_{N-4}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of:  $C_1-C_6$  alkyl,

(16)  $-(CH_2)_{0-4}-CO-O-R_{N-5}$  where  $R_{N-5}$  is selected from the group consisting of:

(a)  $C_1-C_6$  alkyl,

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined

above,

(c)  $C_2-C_6$  alkenyl containing one or two double

bonds,

(d)  $C_2-C_6$  alkynyl containing one or two triple

bonds,

(e)  $C_3-C_7$  cycloalkyl, and

(f)  $-(CH_2)_{0-2}-(R_{1-heteroaryl})$  where  $R_{1-heteroaryl}$  is as

defined above,

(17)  $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(18)  $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$ ,

(19)  $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$ ,

(20)  $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$ ,

(21)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$  where  $R_{N-5}$  can be the same or different and is as defined above,

(22)  $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$ , where  $R_{N-5}$  can be the same or different and is as defined above,

(23)  $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$ , where  $R_{N-5}$  can be the same or different and is as defined above,

(24)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as defined above,

(25)  $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(26)  $-(CH_2)_{0-4}-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(27)  $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(28)  $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$  where  $R_{N-aryl-1}$  is  $-H$  or  $C_1-C_4$  alkyl,

(29)  $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(30)  $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(31)  $-(CH_2)_{0-4}-O-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(32)  $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$  where  $R_{N-5}$  is as defined above,

(33)  $-(CH_2)_{0-4}-S-(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,

(34)  $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, three, four, or five of } -F)$ ,

(35)  $C_3-C_7$  cycloalkyl,

(36)  $C_2-C_6$  alkenyl with one or two double bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(37)  $C_2-C_6$  alkynyl with one or two triple bonds optionally substituted with  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, or

(38)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as described above,

(39)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

(C)  $R_{N-aryl}-W-R_{N-aryl}$ ,

(D)  $R_{N-aryl}-W-R_{N-heteroaryl}$ ,

(E)  $R_{N-aryl}-W-R_{N-1-heterocycle}$ , where  $R_{N-1-heterocycle}$  is the same as  $R_{1-heterocycle}$ , as defined above,

(F)  $R_{N-heteroaryl}-W-R_{N-aryl}$ ,

- (G)  $R_{N\text{-heteroaryl}}\text{-W-}R_{N\text{-heteroaryl}}$ ,  
 (H)  $R_{N\text{-heteroaryl}}\text{-W-}R_{1\text{-heterocycle}}$ ,  
 (I)  $R_{1\text{-heterocycle}}\text{-W-}R_{N\text{-aryl}}$ ,  
 (J)  $R_{1\text{-heterocycle}}\text{-W-}R_{N\text{-heteroaryl}}$ , and  
 (K)  $R_{1\text{-heterocycle}}\text{-W-}R_{1\text{-heterocycle}}$ ,

where W is

- (6)  $\text{-(CH}_2\text{)}_{0-4}\text{-}$ ,  
 (7)  $\text{-O-}$ ,  
 (8)  $\text{-S(O)}_{0-2}\text{-}$ ,  
 (9)  $\text{-N(R}_{N-5}\text{)-}$  where  $R_{N-5}$  is as defined above, or  
 (10)  $\text{-CO-}$ ;

(II)  $\text{-CO-(C}_1\text{-C}_{10}\text{ alkyl)}$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

- (A)  $\text{-OH}$ ,  
 (B)  $\text{-C}_1\text{-C}_6\text{ alkoxy}$ ,  
 (C)  $\text{-C}_1\text{-C}_6\text{ thioalkoxy}$ ,  
 (D)  $\text{-CO-O-}R_{N-8}$  where  $R_{N-8}$  is  $\text{-H}$ ,  $\text{C}_1\text{-C}_6\text{ alkyl}$  or  $\text{-phenyl}$ ,  
 (E)  $\text{-CO-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (F)  $\text{-CO-}R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (G)  $\text{-SO}_2\text{-(C}_1\text{-C}_8\text{ alkyl)}$ ,  
 (H)  $\text{-SO}_2\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (I)  $\text{-NH-CO-(C}_1\text{-C}_6\text{ alkyl)}$ ,  
 (J)  $\text{-NH-CO-O-}R_{N-8}$  where  $R_{N-8}$  is as defined above,  
 (K)  $\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (L)  $\text{-}R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (M)  $\text{-O-CO-(C}_1\text{-C}_6\text{ alkyl)}$ ,  
 (N)  $\text{-O-CO-NR}_{N-8}R_{N-8}$  where  $R_{N-8}$  are the same or different and are as defined above,

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,  
 (P) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two, or three  
 -F, -Cl, -Br, or -I),

(Q) -NH-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), and

(R) -F, or -Cl,

(III) -CO-(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>6</sub> alkyl) where alkyl is optionally  
 substituted with one, two, or three substituents selected from the group consisting of:

(A) -OH,

(B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,

(C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,

(D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or , -phenyl,

(E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different  
 and are as defined above,

(F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different  
 and are as defined above,

(I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,

(K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and  
 are as defined above,

(L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub>s are the same or different  
 and are as defined above,

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(P) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two, or three  
 -F, -Cl, -Br, or -I),

(Q) -NH-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), and

(R) -F, or -Cl,

(IV)  $-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})-\text{S}-(\text{C}_1\text{-C}_6 \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1\text{-C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1\text{-C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different

and are as defined above,

- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different

and are as defined above,

- (I)  $-\text{NH}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and

are as defined above,

- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  are the same or different and are

as defined above,

- (O)  $-\text{O}-(\text{C}_1\text{-C}_5 \text{ alkyl})-\text{COOH}$ ,
- (P)  $-\text{O}-(\text{C}_1\text{-C}_6 \text{ alkyl})$  optionally substituted with one, two, or three

$-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

- (Q)  $-\text{NH}-\text{SO}_2-(\text{C}_1\text{-C}_6 \text{ alkyl})$ , and
- (R)  $-\text{F}$ , or  $-\text{Cl}$ ,

(V)  $-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{\text{N-10}})-(\text{CH}_2)_{0-2}-\text{R}_{\text{N-aryl}}/\text{R}_{\text{N-heteroaryl}}$  where  $\text{R}_{\text{N-aryl}}$  and  $\text{R}_{\text{N-heteroaryl}}$  are as defined above, where  $\text{R}_{\text{N-10}}$  is selected from the group consisting of:

- (A)  $-\text{H}$ ,
- (B)  $\text{C}_1\text{-C}_6 \text{ alkyl}$ ,
- (C)  $\text{C}_3\text{-C}_7 \text{ cycloalkyl}$ ,
- (D)  $\text{C}_2\text{-C}_6 \text{ alkenyl}$  with one double bond,

- (E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,
- (F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and
- (G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above, or
- (VI) -CO-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl) where alkyl is optionally substituted with one or two substituents selected from the group consisting of:
- (A) -(CH<sub>2</sub>)<sub>0-4</sub>-OH,
- (B) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (C) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
- (D) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -phenyl,
- (E) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (F) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (G) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (H) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (I) -(CH<sub>2</sub>)<sub>0-4</sub>-NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,
- (K) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (L) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where R<sub>N-8</sub> are the same or different and are as defined above,
- (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,
- (P) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two, or three -F, -Cl, -Br, or -I),
- (Q) -NH-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), and
- (R) -F, or -Cl;

where  $R_{N-A}$  is selected from the group consisting of H,  $C_1 - C_{10}$  alkyl,  $C_2 - C_{10}$  alkenyl and alkynyl, phenyl,  $C_1 - C_4$  alkyl- $R_{N-aryl}$ ,  $C_1 - C_4$  alkyl- $R_{N-heteroaryl}$ ,  $C_1 - C_4$  alkyl- $C_3 - C_7$  cycloalkyl and  $C_1 - C_4$  alkyl- $R_{1-heterocycle}$ , wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1 - C_3$  alkoxy,  $-C(O)O-R_{1-a}$ , and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H,  $C_1 - C_6$  alkyl or phenyl;

where Z is selected from the group consisting of:

- (A)  $-C(O)-$ ,
- (B)  $-S(O)_{1-2}-$ ,
- (C)  $-C(O)-X_{N-1}-$  where  $X_{N-1}$  is selected from the group consisting of -O-, -S- and  $-NR'-$  and where  $R'$  is as defined above; and
- (D) a single bond;

where  $R_C$  is:

(I)  $C_1 - C_{10}$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1 - C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1 - C_6$  alkoxy, -O-phenyl,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-OC=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-S(=O)_{0-2} R_{1-a}$  where  $R_{1-a}$  is as defined above,  $-NR_{1-a}C=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-C=O NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, and  $-S(=O)_2 NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(II)  $-(CH_2)_{0-3}-(C_3 - C_8)$  cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of  $C_1 - C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1 - C_6$  alkoxy, -O-phenyl, -CO-OH, -CO-O- $(C_1 - C_4)$  alkyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(III)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-x}$  and  $R_{C-y}$  are

- (H) -H,
- (I)  $C_1 - C_4$  alkyl optionally substituted with one, or two -OH,
- (J)  $C_1 - C_4$  alkoxy optionally substituted with one, two, or three -F,

(K)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

(L)  $C_2-C_6$  alkenyl containing one or two double bonds,

(M)  $C_2-C_6$  alkynyl containing one or two triple bonds,

(N) phenyl-, or

(B)  $C_0-C_4$  alkylC(O)  $NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

and where  $R_{C-x}$  and  $R_{C-y}$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-SO_2-$ ,  $-NR_{N-2}-$  and  $R_{C-aryl}$  where  $R_{C-aryl}$  is the same as  $R_{N-aryl}$  and where  $R_{C-aryl}$  may optionally be substituted with  $-C_0-C_4$  alkyl-C(O)  $NR_{1-a}R_{1-b}$ ,  $C_0-C_4$  alkylC(O)  $OR_{1-a}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(IV)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is the same as  $R_{N-heteroaryl}$  and  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(V)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$  where  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$  where  $R_{C-aryl}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(IX)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-heterocycle}$ , and where  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(X)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$  where  $R_{C-heteroaryl}$ ,  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XI)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-aryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$  where  $R_{C-heterocycle}$ ,  $R_{C-heteroaryl}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,



(XIII)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIV)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$ ,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XV)  $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$  where  $R_{C-3}$  is as defined below and  $R_{C-1}$ ,  $R_{C-2}$  are the same or different and are selected from the group consisting of:

(A) -H,

(B)  $-C_{1-6}$  alkyl, optionally substituted with up to three substituents independently selected from the group consisting of  $C_{1-3}$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_{1-6}$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(D)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_{1-3}$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_{1-6}$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(E)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_{1-3}$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_{1-6}$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(F)  $-(CH_2)_{1-2}-S(O)_{0-2}-(C_{1-6} \text{ alkyl})$ ,

(F)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_{1-3}$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_{1-6}$  alkoxy, -O- phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(G)  $-(C_{1-4} \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined for  $R_{1-aryl}$ ,

(H)  $-(C_{1-4} \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,

(I)  $-(C_{1-4} \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(J)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,

(K)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(M)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C'-aryl}$  where  $R_{C-4}$  is -O-, -S- or  $-NR_{C-5}-$  where  $R_{C-5}$  is  $C_{1-6}$  alkyl, and where  $R_{C'-aryl}$  is defined above,

(N)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C-heteroaryl}$  where  $R_{C-4}$  and  $R_{C-heteroaryl}$  are as defined above, and

(O)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above, and where  $R_{C-3}$  is the same or different and is:

(A)  $-H$ ,

(B)  $-C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(C)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(D)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(E)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(F)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,

(G)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,

(H)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(I)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,

(J)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,

or

(K)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(XVI)  $-\text{CH}(R_{C-aryl})_2$  where  $R_{C-aryl}$  are the same or different and are as defined above,

(XVII)  $-\text{CH}(\text{R}_{\text{C-heteroaryl}})_2$  where  $\text{R}_{\text{C-heteroaryl}}$  are the same or different and are as defined above,

(XVIII)  $-\text{CH}(\text{R}_{\text{C-aryl}})(\text{R}_{\text{C-heteroaryl}})$  where  $\text{R}_{\text{C-aryl}}$  and  $\text{R}_{\text{C-heteroaryl}}$  are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to  $\text{R}_{\text{C-aryl}}$  or  $\text{R}_{\text{C-heteroaryl}}$  or  $\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-aryl}}$  or  $\text{R}_{\text{C-heteroaryl}}$  or  $\text{R}_{\text{C-heterocycle}}$  are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH,  $\text{NR}_{\text{N-5}}$ , O, or  $\text{S}(=\text{O})_{0-2}$ , and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one or two  $-\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $=\text{O}$ , or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(XX)  $\text{C}_2\text{-C}_{10}$  alkenyl containing one or two double bonds optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $-\text{O-phenyl}$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(XXI)  $\text{C}_2\text{-C}_{10}$  alkynyl containing one or two triple bonds optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy,  $-\text{O-phenyl}$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(XXI)  $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-6}}\text{-(CH}_2)_{0-1}\text{-R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-aryl}}$  is as defined above and  $\text{R}_{\text{C-6}}$  is  $-(\text{CH}_2)_{0-6}\text{-OH}$ ,

(XXII)  $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-6}}\text{-(CH}_2)_{0-1}\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  and  $\text{R}_{\text{C-6}}$  is as defined above,

(XXIII)  $-\text{CH}(\text{R}_{\text{C-aryl}}$  or  $\text{R}_{\text{C-heteroaryl}})\text{-CO-O}(\text{C}_1\text{-C}_4 \text{ alkyl})$  where  $\text{R}_{\text{C-aryl}}$  and  $\text{R}_{\text{C-heteroaryl}}$  are as defined above,

(XXIV)  $-\text{CH}(\text{CH}_2\text{-OH})\text{-CH}(\text{OH})\text{-phenyl-NO}_2$ ,

(XXV)  $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-O}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-OH}$ ,

(XXVII)  $-\text{CH}_2\text{-NH-CH}_2\text{-CH}(\text{O-CH}_2\text{-CH}_3)_2$ , or

(XXVIII)  $-(\text{CH}_2)_{0-6}\text{-C}(=\text{NR}_{1-a})(\text{NR}_{1-a}\text{R}_{1-b})$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

where  $R_{C-A}$  is H,  $C_1 - C_{10}$  alkyl,  $C_2 - C_{10}$  alkenyl and alkynyl, phenyl,  $C_1 - C_4$  alkyl- $R_{N-aryl}$ ,  $C_1 - C_4$  alkyl- $R_{N-heteroaryl}$ ,  $C_1 - C_4$  alkyl- $C_3-C_7$  cycloalkyl, or  $C_1 - C_4$  alkyl- $R_{1-heterocycle}$ , wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy,  $-C(O)O-R_{1-a}$ , and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H,  $C_1-C_6$  alkyl or phenyl;

where  $R_{C-A}$ ,  $-Z-R_C$ , and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidiny or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1)  $C_1-C_6$  alkyl,

$C_2-C_6$  alkenyl with one or two double bonds, or

$C_2-C_6$  alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1-C_6$  alkyl,

(10) -F, Cl, -Br, or -I,

(11)  $-C_1-C_6$  alkoxy optionally substituted with one, two, or three -F,

(12)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined below,

(13) -OH,

(14)  $-C\equiv N$ ,

(15) =O (oxo),

(16)  $-CO-(C_1-C_4 \text{ alkyl})$ ,

(17)  $-SO_2-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, or

(18)  $-CO-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

or pharmaceutically acceptable salts thereof.

65. A method of treatment according to claim 64, wherein the disease is Alzheimer's disease.
66. A method of treatment according to claim 64, wherein the method is helping prevent or delay the onset of Alzheimer's disease.
67. A method of treatment according to claim 64, wherein the disease is mild cognitive impairment.
68. A method of treatment according to claim 64, wherein the disease is Down's syndrome.
69. A method of treatment according to claim 64, wherein the disease is Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type.
70. A method of treatment according to claim 64, wherein the disease is cerebral amyloid angiopathy.
71. A method of treatment according to claim 64, wherein the disease is degenerative dementias.
72. A method of treatment according to claim 64, wherein the disease is diffuse Lewy body type of Alzheimer's disease.
73. A method of treatment according to claim 64, wherein the method is treating an existing disease.
74. A method of treatment according to claim 64, wherein the method is preventing a disease from developing.

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75. A method of treatment according to claim 64, wherein the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.

76. A method of treatment according to claim 75, wherein the therapeutically effective amount for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.

77. A method of treatment according to claim 76 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.

78. A method of treatment according to claim 64, wherein  $R_1$  is:

$-(CH_2)_{0-1}-(R_{1-aryl})$ , or

$-(CH_2)_{n1}-(R_{1-heteroaryl})$ .

79. A method of treatment according to claim 78, wherein  $R_1$  is:

$-(CH_2)-(R_{1-aryl})$ , or

$-(CH_2)-(R_{1-heteroaryl})$ .

80. A method of treatment according to claim 79, wherein  $R_1$  is  $-(CH_2)-(R_{1-aryl})$  where  $R_{1-aryl}$  is phenyl.

81. A method of treatment according to claim 80, wherein  $R_1$  is substituted with two -F.

82. A method of treatment according to claim 81, wherein the -F substitutions are on the -3 and -5 positions.

83. A method of treatment according to claim 64, wherein  $R_2$  and  $R_3$  are both -H.

84. A method of treatment according to claim 64, wherein  $R_C$  is:

- $C_1$ - $C_8$  alkyl,
- ( $CH_2$ )<sub>0-3</sub>-( $C_3$ - $C_7$ ) cycloalkyl,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-aryl}$ ,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-heteroaryl}$ ,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-heterocycle}$ , or
- cyclopentyl or -cyclohexyl ring fused to  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

85. A method of treatment according to claim 84, wherein  $R_C$  is:

- ( $CH_2$ )<sub>0-3</sub>-( $C_3$ - $C_7$ ) cycloalkyl,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-aryl}$ ,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-heteroaryl}$ ,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-heterocycle}$ ,
- cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

86. A method of treatment according to claim 85, wherein  $R_C$  is:

- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-aryl}$ ,
- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-heteroaryl}$ ,
- cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or  $R_{C-heterocycle}$ .

87. A method of treatment according to claim 86, wherein  $R_C$  is:

- ( $CR_{C-x}R_{C-y}$ )<sub>0-4</sub>- $R_{C-aryl}$  where  $R_{C-aryl}$  is phenyl.

88. A method of treatment according to claim 87, wherein said phenyl is substituted in the 3-position or 3,5-positions.

89. A method of treatment according to claim 64, wherein  $R_{C-A}$  is:

- methyl, or
- ethyl.

90. A method of treatment according to claim 64, wherein Z is:

-C(O)-, or

-C(O)-X<sub>N-1</sub>- where X<sub>N-1</sub> is selected from the group consisting of -O-, -S- and -NR'-.

91. A method of treatment according to claim 64, wherein R<sub>N</sub> is:

-R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> or R<sub>N-heteroaryl</sub> where R<sub>N-aryl</sub> is phenyl where the substitution on phenyl is 1,3-, and where R<sub>N-aryl</sub> or R<sub>N-heteroaryl</sub> are substituted with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub>,

-R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> or R<sub>N-heteroaryl</sub> where R<sub>N-aryl</sub> is phenyl substituted with one C<sub>1</sub> alkyl where the substitution on the phenyl is 1,3,5-, and where R<sub>N-aryl</sub> or R<sub>N-heteroaryl</sub> are substituted with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub>, or

-R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is substituted with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub>.

92. A method of treatment according to claim 91, wherein R<sub>N-2</sub> and R<sub>N-3</sub> are the same and are C<sub>3</sub> alkyl.

93. A method of treatment according to claim 91, wherein R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl substituted with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where the substitution on phenyl is 1,3-.

94. A method of treatment according to claim 91, wherein R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl substituted with one C<sub>1</sub> alkyl and with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where the substitution on the phenyl is 1,3,5-.

95. A method of treatment according to claim 91, wherein X<sub>N</sub> is -CO-, or -SO<sub>2</sub>-.

96. A method of treatment according to claim 95, wherein X<sub>N</sub> is -CO-.



97. A method of treatment according to claim 64 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids: acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

98. A method of treatment according to claim 36 or 64 where the disubstituted amine is selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-({3-  
[(dipropylamino)carbonyl]benzoyl} amino)-2-  
hydroxybutyl}(ethyl)amino)carbonyl} amino)hexanoic acid,  
N<sup>1</sup>-((1S,2S)-1-(3,5-difluorobenzyl)-3-{ethyl[(isobutylamino)carbonyl]amino}-2-  
hydroxypropyl)-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-[(1S,2S)-3-[(butylsulfonyl)(ethyl)amino]-1-(3,5-difluorobenzyl)-2-  
hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-((2S)-2-  
[(isobutylamino)carbonyl]piperidinyl)propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-  
piperazinyl)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,,  
N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[2-(isobutylamino)-2-  
oxoethyl](methyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-  
methyl-2-oxoethyl](methyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]-N<sup>3</sup>,N<sup>3</sup>-  
dipropylisophthalamide, and

~~N<sup>1</sup>-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide.~~

99. A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound according to claim 1.

100. The method of claim 99, wherein said beta-secretase is exposed to said compound *in vitro*.

101. The method of claim 99, wherein said beta-secretase is exposed to said compound in a cell.

102. The method of claim 101, wherein said cell is in an animal.

103. The method of claim 102, wherein said animal is a human.

104. A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound according to claim 15.

105. The method of claim 104, wherein said beta-secretase is exposed to said compound *in vitro*.

106. The method of claim 104, wherein said beta-secretase is exposed to said compound in a cell.

107. The method of claim 106, wherein said cell is in an animal.

108. The method of claim 107, wherein said animal is a human.

109. The method of claims 99 or 104, wherein the compound is selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-({3-  
 [(dipropylamino)carbonyl]benzoyl}amino)-2-  
 hydroxybutyl](ethylamino)carbonyl}amino)hexanoic acid,  
 N<sup>1</sup>-((1S,2S)-1-(3,5-difluorobenzyl)-3-{ethyl[(isobutylamino)carbonyl]amino}-2-  
 hydroxypropyl)-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2S)-3-[(butylsulfonyl)(ethylamino)-1-(3,5-difluorobenzyl)-2-  
 hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{(2S)-2-  
 [(isobutylamino)carbonyl]piperidinyl}propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-  
 piperazinyl)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[2-(isobutylamino)-2-  
 oxoethyl](methylamino)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[1-(1S)-2-(isobutylamino)-1-  
 methyl-2-oxoethyl](methylamino)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]-N<sup>3</sup>,N<sup>3</sup>-  
 dipropylisophthalamide, and  
 N<sup>1</sup>-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-  
 N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide.

110. A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim

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111. The method of claim 110, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

112. The method of claim 110, wherein said reaction mixture is exposed *in vitro*.

113. The method of claim 110, wherein said reaction mixture is exposed in a cell.

114. The method of claim 113, wherein said cell is an animal cell.

115. The method of claim 114, wherein said cell is a human cell.

Sub  
A  
116. A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim 15.

117. The method of claim 116, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

118. The method of claim 116, wherein said reaction mixture is exposed *in vitro*.

119. The method of claim 116, wherein said reaction mixture is exposed in a cell.

120. The method of claim 118, wherein said cell is an animal cell.

121. The method of claim 120, wherein said cell is a human cell.

Sub A1  
122. A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound according to claim 1.

123. The method of claim 122, wherein said administering is to an animal.

124. The method of claim 123, wherein said administering is to a human.

125. A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound according to claim 15.

126. The method of claim 125, wherein said administering is to an animal.

127. The method of claim 126, wherein said administering is to a human.

128. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound according to claim 1.

129. The method of claim 128, wherein said animal is a human.

Sub A1  
130. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound according to claim 15.

131. The method of claim 130, wherein said animal is a human.

132. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound according to claim 1.

133. The method of claim 132, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

134. The method of claim 132, wherein said therapeutic amount is in the range of from about 15 to about 1500 mg/day.

135. The method of claim 133, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

136. The method of claim 135, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

137. The method of claim 133, wherein said disease is Alzheimer's disease.

138. The method of claim 132, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

139. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound according to claim 15.

140. The method of claim 139, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

141. The method of claim 139, wherein said therapeutic amount is in the range of from about 15 to about 1500 mg/day.

142. The method of claim 140, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

143. The method of claim 142, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

144. The method of claim 139, wherein said disease is Alzheimer's disease.

145. The method of claim 139, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

Sub A  
146. A composition comprising beta-secretase complexed with a compound according to claim 1.

147. A composition comprising beta-secretase complexed with a compound according to claim 15.

Sub A  
148. A method for producing a beta-secretase complex comprising: exposing beta-secretase to a compound according to claim 1, or a pharmaceutically acceptable salt thereof in a reaction mixture under conditions suitable for the production of said complex.

149. The method of claim 148, where said exposing is *in vitro*.

150. The method of claim 149, wherein said reaction mixture is a cell.

151. A method for producing a beta-secretase complex comprising: exposing beta-secretase to a compound according to claim 15, or a pharmaceutically acceptable salt thereof in a reaction mixture under conditions suitable for the production of said complex.

152. The method of claim 151, where said exposing is *in vitro*.

153. The method of claim 152, wherein said reaction mixture is a cell.

154. A kit comprising component parts capable of being assembled, wherein at least one component part comprises a compound according to claim 1, enclosed in a container.

155. The kit of claim 154, wherein said compound is lyophilized and at least one further component part comprises a diluent.

156. A kit comprising component parts capable of being assembled, wherein at least one component part comprises a compound according to claim 15, enclosed in a container.

157. The kit of claim 156, wherein said compound is lyophilized and at least one further component part comprises a diluent.

158. A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound according to claim 1.

159. The kit of claim 158, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.

160. The kit of claim 158, wherein each container is adapted for parenteral delivery and comprises a depot product, syringe, ampoule, or vial.

161. The kit of claim 158, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.

162. A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound according to claim 1.

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163. The kit of claim 162, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.

164. The kit of claim 162, wherein each container is adapted for parenteral delivery and comprises a depot product, syringe, ampoule, or vial.

165. The kit of claim 162, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.

166. A kit comprising a compound according to claim 1; and  
one or more therapeutic agent selected from the group consisting of an antioxidant, an anti-inflammatory, a gamma secretase inhibitor, a neurotrophic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody.

167. A kit comprising a compound according to claim 15; and  
one or more therapeutic agent selected from the group consisting of an antioxidant, an anti-inflammatory, a gamma secretase inhibitor, a neurotrophic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody.

168. A composition comprising a compound according to claim 1; and an inert diluent or edible carrier.

169. The composition of claim 168, wherein said carrier is an oil.

170. A composition comprising a compound according to claim 1; and an inert diluent or edible carrier.

171. The composition of claim 170, wherein said carrier is an oil.

172. A composition comprising a compound according to claim 1; and a binder, excipient, disintegrating agent, lubricant, or gildant.

173. A composition comprising a compound according to claim 15; and a binder, excipient, disintegrating agent, lubricant, or gildant.

174. A composition comprising a compound according to claim 1 disposed in a cream, ointment, or patch.

175. A composition comprising a compound according to claim 15 disposed in a cream, ointment, or patch.

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